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IS THERE AN ANTAGONISM BETWEEN THE MALE AND THE FEMALE SEX-ENDOCRINE GLAND?

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The suggestion of Steinach that an antagonism exists between the male and the female sex glands has been discussed by different authors. Recently Moore, basing his opinion on the experimental work of himself and of his pupil Fisher, came to the conclusion that the assumption of an antagonism has to be rejected (1).

Experimental work which I have done during the past two years with my coworkers, first with W. Krause and H. E. V. Voss, later on with F. Lange, M. Tiitso, H. Perli and D. Svikul, made it evident that the position as held by Moore is by no means justified.

First of all Moore does not discriminate between two different meanings of "antagonism." Steinach spoke of an antagonism of the sex glands in the sense that the taking and the survival of the heterosexual graft is inhibited by the glands in situ. According to Steinach the taking and the survival of the heterosexual graft is possible only when the glands in situ are removed and, as in his experiments with hermaphroditism, reengrafted simultaneously with the heterosexual gland. Sand succeeded in producing experimental hermaphroditism engrafting the ovaries in the testicles in situ, thus injuring the latter

to a certain degree. But Schultz, Moore and Fisher have shown that both taking and survival of the opposite-sexed graft is really possible when one or even both uninjured glands in situ are present. But on the other hand, Steinach suggested that there is an antagonism in the sense also that the sex gland inhibits the characters of the opposite sex by its sexual hormones. As to the second meaning of antagonism the numerous experiments of Goodale and Pézard which have been fully confirmed by Zawadowsky, have shown that such an inhibiting influence really exists (plumage, spurs). This affords, as I think, another possibility of antagonism, i.e., that the heterosexual graft survives, but that its *hormonic effect* is inhibited by the glands in situ. Our own experiments have shown that the last supposition is true.

In the following paragraphs are reported the new data we have obtained in experiments on hermaphroditism in guinea-pigs. Only part of this work has as yet been published (2). Detailed papers are in course of publication.

(1) Ovarian and testicular fragments survive for several months, even in presence of two glands of the opposite sex, and can perform their endocrine function.

(2) But possibility of survival does not mean that the presence of the heterosexual glands is of no influence This is best shown by two comparative series of experiments: (a) Out of sixteen animals into which one to two ovaries were engrafted by the intratesticular method of Sand, both testicles remaining in the body, only four revealed a feminine hormonic effect (hypertrophy of the mammary glands and nipples), whereas six experiments with intratesticular ovarian grafts and unilateral testicular castration revealed a feminine hormonic effect *without any exception.* (b) Seventeen male guinea pigs with testicular fragments were engrafted intrarenally with ovarian fragments (from one-fourth to two ovaries); all of these animals, with one exception, revealed a feminine hormonic effect.

(3) Fourteen guinea pigs were engrafted with ovaries by the intrarenal method, both testicles remaining in situ; there was not a single case with a feminine hormonic effect, though the animals were observed sometimes more than five months.

It suffices to compare the result in 2b with that in 3 to understand how great is the influence of the testicle in situ on the hormonic effect of the ovarian graft. But still more evidence is given by the experiments mentioned in paragraph 4.

(4) The left ovaries of five guinea pigs were engrafted by the intrarenal method into five males having both testicles in situ; the right ovaries of the same females were engrafted by the same method into five males which were of the same age as the first group, but had previously undergone partial castration, only testicular fragments being now present in the body. No animal of the first group revealed a feminine hormonic effect, whereas all the animals of the second group did. Here the ovary of the same female was capable of producing a striking hormonic effect when the testicle was reduced to a fragment, but was unable to do so when both testicles were present.

(5) The antagonistic influence exhibited by the testicle is evident even in those cases in which the hormonic effect of the ovarian graft is not definitely inhibited. In the intratesticular experiments of Sand and of Krause with both testicles remaining in the body, the *time of latency*, i. e., the time between ovarian transplantation and the beginning of the feminine hormonic effect, was five to eighteen weeks. In our experiments in which only testicular fragments were present, or in which a testicular castration was made, the time of latency was in general fourteen days, only in two animals three to four weeks.

(6) There is no possibility that our results were caused incidentally by an especially favorable age of the males or females used in the experiments. We have shown that the advanced age of the male into which an ovarian graft is made, and the youth of the female from which the ovary is taken, do not influence much the result of the experiment. We succeeded in causing a feminine hormonic effect, even with milk secretion, in fully grown males weighing up to 845 gm.; we succeeded in causing a feminine hormonic effect by engrafting ovaries of animals only seventeen days old. The time of latency was in all these experiments again only two weeks.

(7) The short time of latency was not caused by the fact that a special place (the kidney) was chosen for the ovarian

graft. We have succeeded in causing a hormonic effect in a male with a testicular fragment by engrafting the ovary in the abdominal cavity, the time of latency being again about two weeks, as in the intrarenal experiments.

(8) The definite proof that the testicle can inhibit the hormonic effect of the ovarian graft is given by those experiments which may be best designated as *unbolting experiments:* (a) An animal having both testicles in situ and an ovary in the kidney showed as usual no feminine hormonic effect, whereas an animal with a testicular fragment and the second ovary of the same female revealed a feminine hormonic effect in less than two weeks. Now, seven weeks after the ovarian transplantation, both testicles were removed in the first animal, and eleven days later there was a striking hormonic effect. (b) Nine males with both testicles in situ were engrafted by the intrarenal method with one ovary each. There was no feminine hormonic effect three to eight weeks later. Now, from five animals both testicles were removed; four to ten days after testicular castration a feminine hormonic effect set in in four of these animals, whereas the uncastrated animals remained negative. This is really an *experimentum crucis* leaving no doubt as to the inhibiting influence of the testicle on the ovarian graft.

(9) It is of the greatest interest that not only operative reduction of the testicular mass but also operative interference alone on the testicle is capable of "unbolting." This is shown by the following experiment. In three males resection of the cauda epididymidis was made, and an ovary was engrafted into the kidney; all three males revealed a feminine hormonic effect. The testicles were found fixed by adhesions in the abdominal cavity. The time of latency was from about two and a half weeks to two and a half months.

(10) The unbolting effect can be obtained also by causing experimental cryptorchidism in a male engrafted with ovary, without resection of the epididymis. Five males were engrafted with ovaries by the intrarenal method and a few days later both testicles were fixed in the abdominal cavity to cause cryptorchidism. Three animals revealed a feminine hormonic effect. The time of latency was about three weeks.

After all these observations there can be no doubt that *the hormonic effect of the engrafted ovary depends also upon the quantity and the condition of the testicular mass simultaneously present.* There are cases in which the ovary survives and reveals follicular development, notwithstanding the presence of both testicles in situ, but there is then no feminine hormonic effect. *When discussing the "antagonism" between the sex glands it is absolutely necessary to discriminate between the survival of the graft and its hormonic effect.*

There are, however, at first sight some discrepancies. There was a feminine hormonic effect in the intratesticular experiments of Sand in about twenty per cent of the cases, notwithstanding the presence of both testicles. There were sometimes positive cases even when Krause engrafted by the intratesticular method only an ovarian fragment, both testicles remaining in the body. On the other hand, the intrarenal experiments which gave about one hundred per cent positive cases in animals with testicular fragments were always negative when both testicles remained in situ. How is this contradiction to be explained? Sand is of the opinion that the position of an intratesticular ovarian fragment is as to nutrition different from that of an ovarian fragment engrafted wherever it may be. But according to our experiments the explanation is quite another one. There is no doubt that the twenty per cent of positive cases in the intratesticular experiments with both tesicles in the body were caused by operative interference on the testicle of the engrafted animal; in most of the positive intratesticular experiments of Sand and of Krause one or both testicles were involuntarily fixed by adhesions in the abdominal cavity; the condition was quite the same as in our intrarenal experiments with experimental cryptorchidism (see paragraph 10). That the abnormal position of the testicle is the unbolting factor is shown also by another set of experiments.

(11) In four male animals engrafted with one ovary each, a bilateral resection of the epididymis or a bilateral ligature of the vas deferens was made *by the scrotal route* so as to exclude experimental cryptorchidism. There was no feminine hormonic effect during six to eight weeks of observation. Removal of the testicles was then performed in two of the animals with resec-

tion, and in one the feminine hormonic effect set in four days later.

(12) In the same way as the feminine hormonic effect of the ovary is inhibited by the testicles in situ, *the masculine hormonic effect of a testicular fragment can be inhibited by an ovarian graft,* though this is not always necessarily the case. In experiments with Voss we found twice, in males with ovarian grafts and a positive feminine hormonic effect, the presence of testicular fragments with ripe spermatozoa, whereas the male sex stigmata were characteristic for a castrated animal. I *never* saw a similar coincidence in numerous cases of partial castration in guinea pigs in which testicular fragments *alone* were present.

At the moment it is not possible to give a definite explanation of the mechanism underlying the inhibitory influence which the testicle in situ has on the hormonic effect of the ovarian graft. It is not probable that the hormone production of the ovary is always inhibited in these cases, since it has been shown by different authors that the ovarian graft which does not exhibit an hormonic effect can reveal follicular development. This is shown also by our statement that in the unbolting experiment (see paragraphs 8 and 11) the feminine hormonic effect began within a *few days* after the removal of the testicles from the engrafted animal. There was even a case in which the feminine hormonic effect set in in less than two days after unbolting. The same is shown also by the following observation.

(13) We examined *simultaneously* the condition of the ovaries of the *same* female in an animal with both testicles in situ in which there was no feminine hormonic effect, and in an animal which revealed a feminine hormonic effect a few days after unbolting. *The ovaries were quite identical in both animals.*

Our experiments in which the displacement of the testicles to the abdominal cavity were "unbolting" factors make it highly probable that some processes going on in the seminiferous tubules are in play in the inhibiting action of the testicle. But the question is a quite difficult and delicate one, as shown by the following two statements.

(14) In an engrafted animal with bilateral resection of the epididymis in which there was for eight weeks no feminine hormonic effect, the testicles were removed and four days later a feminine effect set in (see paragraph 11). Microscopical observation revealed that in both testicles the seminal tubules were highly reduced. In this case the testicles were able to perform their antagonistic influence though the seminal tubules revealed no signs of spermatogenesis.

(15) The mechanism underlying the unbolting effect of experimental cryptorchidism seems to be quite a special one. This is shown by the following two sets of experiments. (a) Twenty-one unilaterally castrated male guinea-pigs were intrarenally engrafted with ovaries; there was a feminine hormonic effect in five cases, but the time of latency was of five to seven *months*. (b) In thirteen male guinea-pigs a unilateral cryptorchidism was caused, the second testicle remaining intact in situ. The animals were intrarenally engrafted with ovaries. A feminine hormonic effect set in in three cases already about six *weeks* after the operation. It is clear that the presence of a retained testicle, besides the normal one, is a factor which favors the feminine hormonic effect. It is very likely that substances originating in the degenerating seminal tubules are here in play influencing the somatic substratum which becomes more able to react to ovarian hormones notwithstanding the presence of the second intact testicle.

Our experiments as yet lead to no definite conclusion of the question whether the antagonistic influence of the testicles in situ on the ovarian graft or on the hormonic effect of the latter and *vice versa* is a sex-specific one, caused by sexual hormones.

(16) Finally another set of experiments may be mentioned which showed that the hormonic effect of an ovarian graft depends not upon resorption of hormones already present in the ovary at the time when the graft is made, but upon hormones produced in the surviving graft. There was never a feminine hormonic effect in those experiments in which rabbits' ovaries were engrafted into the kidney of male guinea pigs, the ovarian grafts not taking and undergoing degeneration.

Our experiments, which number more than one hundred and fifty, show that the problem of the antagonistic influence

between the sex glands is by no means negatively settled as Moore has claimed.

BIBLIOGRAPHY

1. Moore: Science (Utica), 1924, **59**, 41.
2. Lipschütz & Krause: Compt. rend Soc. de biol. (Par.). 1923, **89**, 220; 1135.
Krause: Deutsche med. Wchnschr., 1923, **49**, 1330.
Lipschütz, Krause & Voss: J. Physiol. (Lond.), 1924, **58**, 461. 1141; 1239; 1332; 1410; **91**, 868.
Lipschütz & Voss: Compt. rend. Soc. de biol. (Par.), 1924, **90**, 1139;
Lipschütz: Klin. Wchnschr., 1924, **3**, 1903.
Lipschütz: Rassegna di Studi Sessuali (Roma), 1924, **4**, 297.
Lipschütz: Compt. rend. Soc. de biol. (Par.), 1924, **91**, 865, 870.
Lipschütz: J. Physiol. (Lond.), 1924, **59**, 333.

STUDIES ON THE PATHOLOGY OF THE HYPOPHYSIS
V. ABSCESS OF THE HYPOPHYSIS

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Abscesses found in hypophyses removed at necropsy are usually only incidents in the course of a fatal acute infection occurring in some adjacent or distant part of the body. Such lesions thus discovered do not, *per se,* possess much practical clinical significance. Any clinical manifestations attributable to the suppurative process in the hypophysis either would not have time to display themselves, or they would be overshadowed and obscured by the more marked symptoms of the disease which was the immediate cause of death. However, from a study of such cases something may be learned of the etiology, pathogenesis and most common location of this lesion. Inasmuch as not all acute infections, such as are often found on postmortem examination to be complicated by abscess of the hypophysis, are fatal, a study of the conditions giving rise to this pathologic change may aid in the interpretation and explanation of some obscure cases of hypopituitarism. For this reason it has been thought that the following review of the literature and a report of seven new cases might be of some value and therefore warranted.

The first recorded case of abscess of the hypophysis appears to be that reported by Heslop in 1848 (1). Glinski (2) has reported a case of suppuration of the hypophysis in a 40 year old woman who died of pyemia two weeks after childbirth. Schmorl (3) mentioned abscess of the hypophysis as an accompaniment of "embolic processes associated with sepsis." M. Simmonds (4), in a paper on embolism of the hypophysis, reported four cases of abscess, and made the startling statement that "in the anterior lobe bacterial emboli may remain without effect or they may cause anemic infarcts, while in the posterior lobe they lead to the formation of abscesses." Plaut (5) has

taken exception to the first part of this statement, and reported nine cases of abscess of the hypophysis. In five cases the lesions were multiple, and all were located in the neurohypophysis. Four of his cases followed abortion with septic thrombosis; two were associated with osteomyelitis with thrombophlebitis; two complicated malignant endocarditis; and one occurred as part of a general septicemia. Schaefer (6) reported metastatic abscesses in all three lobes of the hypophysis in a soldier who died of streptococcus septicemia following a gunshot wound of the knee. He also described a perihypophyseal abscess in a case of generalized staphylococcus infection.

Cases of acute suppurative hypophysitis complicating purulent sphenoidal sinusitis have been reported by Harvey (7), Meyer (8), and Boggs and Winternitz (9). Glinski (2), Smoler (10), Thom (11) and Plaut (5) have reported abscesses in the anterior lobe of the hypophysis as an accompaniment of purulent leptomeningitis.

In my series of over two hundred hypophyses examined in serial sections, seven instances of abscess have been found. Six of these were in the anterior lobe, and one in the posterior lobe. A brief summary of these cases follows:

Case 1. White male, about 65 years old. Death was due to subdural hemorrhage possibly resulting from trauma. The hypophysis was about one and one-half times the normal size. Within the capsule in the median plane of the anterior surface was an abscess large enough to occupy more than one low power field of the microscope. The interstitial tissue of the anterior lobe immediately beneath the abscess was infiltrated with polymorphonuclear leucocytes.

Case 2. Thirteen year old white boy. There were bilateral suppurative otitis media and mastoiditis complicated by purulent leptomeningitis. Beneath the capsule on the front of one lateral half of the anterior lobe of the hypophysis was an abscess about one-fourth the size of the entire lobe.

Case 3. Well nourished white male, 11 years old. Acute suppurative otitis media was complicated by purulent leptomeningitis. The hypophysis was about one and one-half times the normal size. Almost one entire lateral half of the anterior lobe had been destroyed by an abscess.

Case 4. Well nourished colored female, aged 39 years. Evidence of lobar pneumonia, acute fibrinous pleurisy, acute pneumococcus leptomeningitis, ulcerative aortic endocarditis and acute glomerulonephritis was observed. The hypophysis was very slightly enlarged. Immediately beneath the capsule of the hypophysis was a zone of infiltration with polymorphonuclear leucocytes extending around almost the entire periphery of the gland. From each side the infiltration dipped in between the anterior and posterior lobes, separating these structures and more or less completely destroying the middle lobe.

Case 5. Female, 33 years old. There were serofibrinous pericarditis, fibrinopurulent leptomeningitis, multiple abscesses of the brain, hypostatic bronchopneumonia, acute suppurative tracheobronchial and mediastinal lymphadenitis. The hypophysis was slightly enlarged. In the anterior part of the anterior lobe was an extensive subcapsular abscess involving about one-third of the anterior lobe, and situated chiefly lateral to the median plane.

Case 6. Poorly nourished white female, 46 years old. There were caseous tuberculosis of the right lung, chronic fibrous and acute fibrinopurulent pleurisy on the right side, unhealed thoracostomy wound, purulent leptomeningitis and ependymitis, and multiple small abscesses of the brain. The hypophysis was about normal size. Just beneath the capsule at one antero-lateral border was a small, roughly triangular abscess, about the size of one low power field of the microscope. Surrounding the abscess on two sides was a zone of hyperemia in which the interstitial tissue was infiltrated with polymorphonuclear leucocytes.

Case 7. White male, aged 26 years. Examination showed ulcerative mitral and mural endocarditis, multiple anemic infarcts of the kidneys and spleen, and multiple small septic infarcts of the brain. In one antero-lateral quadrant of the posterior lobe of the hypophysis was a small abscess about the size of one low power field of the microscope.

The etiology of the abscess in the capsule in Case 1 is not clear. No clinical history was obtainable, and the circumstances under which the necropsy was done made a satisfactory examination of the associated pathological conditions next to impossible. The remaining six cases illustrate the two distinct ways in which abscess of the hypophysis may originate, namely, by the lodgement of mycotic or septic emboli, and by extension from a suppurative inflammation of nearby structures.

Case 7 was definitely, and Cases 5 and 6 probably, of embolic origin. In the two last mentioned cases purulent leptomeningitis was present, but each showed also multiple "metastatic abscesses" in the brain. In Case 6 the abscess was wedge-shaped and, therefore, had the form of an infarct. Furthermore, in each instance, the purulent infiltration of the capsule was less marked than in the other cases with meningitis. It is at least possible, therefore, that septic emboli may give rise to abscesses in the anterior, as well as in the posterior, lobe. Case 6 is especially interesting in this connection. There were no vegetations on the heart valves. It is well recognized that bronchiectasis and other inflammatory conditions of the lungs may be complicated by multiple abscesses of the brain. This case suggests the possibility that these diseases may also give rise to abscess of the hypophysis. It is this group of embolic abscesses that is of special interest to the endocrinologist. For these

patients have at least a chance of recovery, and may later show otherwise unexplainable evidences of deficiency of function of the pituitary.

The group of hypophyseal abscesses complicating purulent leptomeningitis (Cases 2, 3 and 4) is interesting chiefly because of the mechanism by which the infection reaches this gland. These abscesses are most commonly situated immediately beneath the capsule in one of the antero-lateral quadrants of the anterior lobe. In a later paper it is hoped to present some observations on the blood supply of the hypophysis. Suffice it to state here that two fairly large arteries enter the front of the anterior lobe, one on either side, and at a little distance from the sagittal plane. These vessels penetrate the glandular portion of the hypophysis and pass to the rich plexus of vessels in the core of connective tissue which is located at about the center of each lateral half of the anterior lobe. The infection appears to enter the hypophysis along one or the other of these blood vessels, perhaps by way of the perivascular lymphatics. In this connection, the case of Boggs and Winternitz (9) is of special interest because the primary focus of infection was in the sphenoidal sinus and probably reached the hypophysis, without involving any other structures, by the route just mentioned. In Case 4, the abscess was located between the anterior and posterior lobes. The infection probably gained access to the hypophysis along blood vessels which Benda (12) has described as entering the lateral surface and passing medialward between the neurohypophysis and the glandular portion.

SUMMARY

1. Seven new cases of abscess of the hypophysis are reported and the mechanisms by which the infection reaches this gland are described.

2. Abscess of the hypophysis may be embolic in origin and may involve either the anterior or posterior lobes or both. It may occur as a complication of acute endocarditis, pyemia, or bronchiectasis and chronic inflammatory processes in the lungs and pleura. Such diseases are not invariably fatal, and patients recovering from them may later show evidences of hypopituitarism.

3. Abscess of the hypophysis is a not very infrequent complication of purulent leptomeningitis. The lesion in these cases is usually located just beneath the capsule in one antero-lateral quadrant of the anterior lobe. The infection appears to enter the gland along the perivascular lymphatics of one or both of two blood vessels which enter the anterior surface of the anterior lobe lateral to the median plane. Or it may enter along blood vessels which penetrate the lateral surface, and the abscess then develops between the anterior and posterior lobes.

BIBLIOGRAPHY

1. Heslop, T. P.: A case of hypertrophy with abscess of the pituitary body. Dublin Quart. J. M., 1848, **6**, 466.
2. Glinski, L. K.: Anatomische Veraenderungen der Hypophyse. Przegl. lek. (Kraków), 1913, No. 1; abst. in Deutsche med. Wchnschr. (Leipz. & Berl.), 1913, **39**, 473.
3. Schmorl: Discussion on the pathology of the hypophysis. Verhandl. d. deutsch. path. Gesellsch. (Jena), 1914, **17**, 231.
4. Simmonds, M.: Ueber embolische Prozesse in der Hypophyse. Arch. f. path. Anat. [etc.] (Berl.), 1914, **217**, 226.
5. Plaut, A.: Hypophysenbefunde bei akuten Infektionskrankheiten. Arch. f. path. Anat. [etc.] (Berl.), 1922, **237**, 165.
6. Schaefer, H.: Beitrag zur Lehre von den Entzuendungen spezifischer und nicht spezifischer Natur in der Hypophyse. Diss., Path. Inst. (Jena), 1919.
7. Harvey, J. R.: Sudden and complete amaurosis; scrofulous tumor compressing the optic nerves; abscess of the pituitary gland; caries of the body of the sphenoid bone. Dublin Quart. J. M., 1855, **20**, 220.
8. Meyer, O.: Demonstration einiger seltener Praeparate von Hirntumoren und Erkrankungen der Hypophysengegend. Ztschr. f. Psychiat. (Berl.), 1918, **74**, 521.
9. Boggs, T. R., & Winternitz, M. C.: Acute suppurative hypophysitis as a complication of purulent sphenoidal sinusitis. Johns Hopkins Hosp. Rep. (Balt.), 1919, **18**, 56.
10. Smoler, F.: Ueber ein operierten Fall von zystischen Hypophysen tumor. Prag. med. Wchnschr., 1914, **39**, 71.
11. Thom, W.: Untersuchungen ueber die normale und pathologische Hypophysis cerebri des Menschen. Arch. mikr. Anat. u. Entwckl. (Bonn), 1901, **57**, 632.
12. Benda, C.: Pathologie der Hypophysis cerebri. Flatau-Jakobson's Handb. d. path. Anat. d. Nervensystems (Berl.), 1904, p. 1429.

CASE REPORT OF A PSEUDOHERMAPHRODITE

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Instances of malformation of the genital organs of such degree as to bring into question the sex of the afflicted individual are still sufficiently uncommon to warrant the report of instances as they may be encountered. The present case is that of a child aged 20 months, who, 22 hours before death, was admitted to the hospital in coma. The parents stated that the genital abnormality was recognized at birth and that after deliberation the physician in attendance decided that the individual was a boy. Aside from the genital condition there were no stigmata of endocrine defect in evidence.

Post-mortem examination revealed the cause of death to be chronic interstitial nephritis with small granular kidneys of the type usually seen in those dying in advanced age. Histological examination of the kidneys showed advanced glomerular fibrosis, marked increase in the kidney stroma, and vascular sclerosis approaching obliteration of the vessels. Accompanying this was cardiac hypertrophy, the left ventricle wall measuring 1.6 cm. in diameter.

Inspection of the genital organs showed what appeared to be a penis 3 cm. in length, covered by a foreskin which could be retracted. Situated 0.5 cm. below the root of the penis was an opening 0.6 cm. in diameter from which urine was said to have escaped. This opening pouted and on the lower wall, 0.3 cm. from the cutaneous edge, was an opening through which a probe could be passed into the vagina. Embracing but not concealing the penis were two labia having the characteristics of the labia majora; the labia minora were absent.

Lying behind the bladder was the vagina, 3.6 cm. in length, which, except for a minute opening, ended blindly against the urethral wall. Into the vagina there projected a uterus, 4.2 cm. in length, which was completely divided by a septum from cervix to fundus. There was no definite tubal formation, the

uterine horns being prolonged so as to form tubes; these prolongations were 4 cm. in length. One cm. from the distal end of the left tube was an ovoid pearly white body 1 cm. in length,

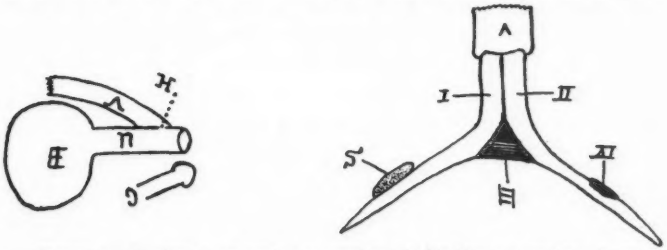

Figure 1. C, clitoris or penis; u, urethra; b, bladder; v, vagina; h, opening of vagina into urethra; I and II, body of uterus with septa; s, testes; III, muscular wall of uterus; IV, masculine genital remnants.

and on the opposite tube at the same location there was a thickening of the wall.

Histological examination of the vagina showed the epithelial lining to be normal. The uterine body and tubal extensions

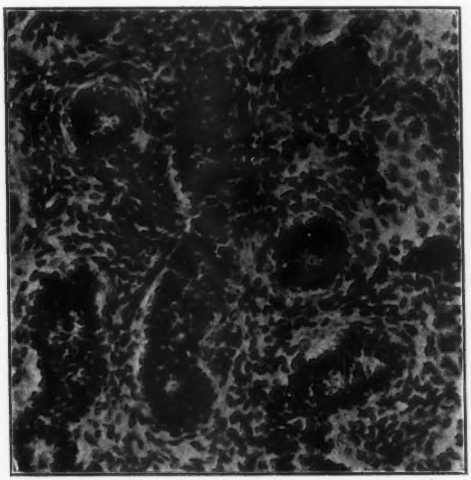

Figure 2. Photomicrograph; X 250. Embryonic testis attached to uterine horn.

were lined by stratified squamous epithelium and were devoid of glandular structure. The thickening of the right tubal wall

was shown to be due to an island of tissue, apparently the vas deferens, adjacent to which was a small canal lined by columnar epithelium (spermatic cord?). The ovoid body attached to the left tubal extension was an embryonal testis, the histological features of which are shown in the accompanying photomicrograph. There were no abnormalities of any of the other endocrine glands.

SUMMARY

The case is reported of an individual with the external genitals resembling the male and the female and with internal genital organs consisting of a bicornate uterus with a septum, and one gonad, an embryonal testis, a portion of the vas deferens and a spermatic cord.

THE EFFECT OF FEEDING FOWLS ON THYROID GLAND

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Although the literature contains many reports of thyroid treatment in numerous species of animals, the only work found on thyroid feeding in fowls is that of C. J. and C. Parhon.* These investigators observed as a result of thyroid treatment marked excitability, tremors and complete ischemia of the comb. Increased resistance to fowl cholera was also reported.

The observations herein reported were begun in the summer of 1919 at the Zoological Gardens of New Ascania in South Russia, under the guidance of Prof. Michael Zavadovsky. The work was continued during 1919 and 1920 in the laboratory of Prof. B. P. Babkin at Odessa. From the fall of 1920 on, the work has been continued at our own laboratory at Moscow. During this period over sixty fowls have been experimented upon, not including controls.

METHOD OF INVESTIGATION

The method of the experiments consisted in feeding the fowls on thyroid gland. The glands were taken from domestic animals and obtained directly from the slaughter house; in Ascania Nova they were from sheep, in Odessa from cattle, and in Moscow from horses mostly. Poehl's desiccated tablets and Parke-Davis preparations were also used. Most recently lumps of desiccated gland prepared in the winter of 1923 from thin slices of horse glands in a thermostat at a temperature of 50° to 60° celcius were employed.

It was only last August (1923) that by the kindness of Dr. Sandberg of Chicago a small quantity of thyroxin was obtained. Its action proved to be identical with that of the fresh glands. However, circumstances do not permit a detailed consideration of these experiments with thyroxin and a closer analy-

*Parhon, C. J., & Parhon, C.: Note sur l'hyperthyroïdisation chez les oiseaux et sur la résistance des animaux ainsi traités aux infections spontanées. Compt. rend. Soc. de biol. (Par.), 1914, **76**, 662.

sis of the results of the experiments until the next report. In this paper the effect of thyroid gland on the fowl's organism from various points of view will be dealt with.

The doses at first were large enough to produce rapid results of acute and even fatal poisoning, varying from one to twelve sheep glands or from one to one and a half beef or horse glands.

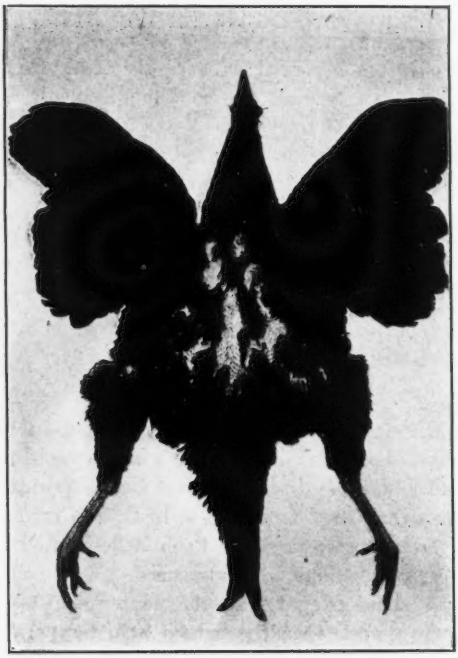

Figure 1. The cock of bred "Minor" in the state of moulting.

As controls part of the fowls during the first experiments were given an equal or even larger amount of meat. But it has now been demonstrated beyond all doubt that the symptoms described are attributable specifically to the action of the thyroid, and not to meat in general. Such control experiments no longer seem necessary. As occasion arises all further variation and changes in the method employed will be duly noted.

RESULTS

Experimental moulting. The accelerated moulting that within a short time all but strips a bird bare is one of the most striking and evident symptoms of hyperthyroidism. Three or four days after the commencement of the treatment are sufficient to weaken the roots of the feathers so that they fall out easily every time the bird is handled. In eight to ten days the feathers begin to fall out of themselves. The moulting is the more pronounced, the larger the doses, and can be so severe that the whole yard is strewn with feathers, and the bird goes about entirely naked. The intensity and rapidity with which moulting sets in varies slightly with the quantity of gland administered, but, generally speaking, it begins within eight to ten days.

The growth of white feathers. The very first experiments showed that under the influence of thyroid feeding completely black fowls produced in place of the moulted black feathers a new plumage with an abundance of white feathers. This was true not only of the wing feathers which are generally very susceptible to blanching even in thoroughbreds but to the body feathers also, converting the pure black fowls to a greater or lesser degree to spotted. In a second series of experiments an identical result was obtained in black fowls having at the beginning not a trace of white on them. This whitening regularly takes place in all instances in twenty-five to twenty-seven days after the first administration.

Acute poisoning. In all the experiments already described mostly very large doses of thyroid gland, approximately three to six sheeps' gland a day, were given. A quantity exceeding six glands was enough to cause marked depression. The cock would sit with ruffled feathers on one spot, or stroll listlessly about the yard, his wings hanging slightly down. While in this state the bird moulted very actively. In such cases unless the thyroid feeding was discontinued or if the dose was increased to ten to twelve glands, curious convulsive fits that terminated in death were observed. The phenomena of poisoning have been so similar in my experiments that the description of one instance will be sufficient.

Experiment No. 6. Langshan cock, halfbred white, age four to five months. The experiment began on July 13, 1919. Thyroid glands —four to eight daily—were administered for a period of eight days, amounting to fifty-two glands in all. On July 21 a plentiful moult

was in progress. The next day twelve glands were administered; on the next, ten. On July 24 several interesting changes in behavior were noted; it had previously been very shy, but had now become quite tame. Two thyroid glands were offered to it, of which it ate only one, pecking off the mark and with no assuredness. One hour later it was found lying exhausted in the middle of the yard. When lifted, after a few steps taken with difficulty, it fell down again. It would not peck at any grains. One hour later it was observed again lying in the same position on its side, with its legs stretched out. During the next two hours it had several attacks of convulsions at intervals of five to ten minutes. Death then ensued.

The foregoing experiment might be regarded as inconclusive, there being a possibility that the color changes observed were not attributable to the thyroid feeding, but were merely incident to growth, as often happens with fowls. A further study was therefore carried out, upon thoroughbred black fowls.

A pure black cock was kept in a state bordering on poisoning from beef thyroid glands (obtained from the slaughter house) over four months, except for a few intermissions when it was fed with milk, wheat bread and the like. Within three months (December 11, 1919, to March 9, 1920) it was made at will to moult completely, each time developing a larger plumage of white feathers and a very decided thinning of the black pigment in what remained.

In accordance with the instant at which a given plumage was obtained it was possible to secure on a general background of scanty black feathers a new plumage sometimes pure white, sometimes black tipped with white, a condition abnormal in fowls.

The following abridged protocol will give some idea of the course of the experiment.

Experiment No. 12 at Odessa. On Dec. 11, 1919, two Langshan cocks and three hens five to six months old were purchased. They had not yet moulted. The cock only was fed thyroid, the others being provisionally kept as control birds.

From Dec. 11 to 16, inclusive, the cock was given nine beef glands, i. e. one and a half a day. On Dec. 17 a depressed condition was observed. The dosage was then cut down to one-sixth to one-eighth of a gland. On July 18 the cock remained motionless, incapable of eating or drinking unaided. Food placed in the throat was swallowed greedily. When its beak was thrust into a cup of water it drank eagerly. Towards the end of the meal it tried to drink for itself but missed the basin when it bent its head. It then tried to peck but did not even touch the floor. The feathers were dropping in huge quantities, bestrewing the whole floor. It had lost much flesh; the crop was empty. On Dec. 20 the condition was much the same, though the cock was livelier and sometimes pecked successfully. On Dec. 24, 1921, the condition was improved: as before, no gland was administered. It now pecked vigorously but at the observer's

trousers, fingers, etc., and anything else except the grain held out in the hand. It often pecked ridiculously at the air, missing the food which was some little distance away. The feathers continued to fall in heaps.

On Dec. 25 the cock had lost nearly all its feathers. Otherwise it had recovered completely save for its eyesight. It was again given half a gland, and this provoked a condition of severe illness. The administration of thyroid gland was discontinued until Dec. 31.

Dec. 29, systematic measurements were begun on the cock and on the control hen. The cock, which was at first larger than the hen, now weighed 1650 gm. against 1810 gm. for the hen. From Dec. 31 to May 1 the cock was given one-sixth to one-fourth of a gland daily and it increased in weight. The control hen began to moult normally.

On Jan. 6, 1921, young white feathers were noticed for the first time on the breast and tail among many black stumps. But the new growth was slow and the quills were crumpled. The dose was raised to half a gland daily.

By Jan. 7 a large number of white feathers had appeared on various parts of the body. From Jan. 8 to 17 a quarter to a third of a gland was daily administered, with occasional interruptions. During this period the bird was again slightly ill. The young black feathers that had begun growing densely on the back and elsewhere gradually turned purplish-grey.

The appearance suggested that the production of pigment had entirely ceased and the old stock of pigment was being distributed over a larger surface in proportion to the growth of the plumage. Some feathers were purplish-black at the tip, but pure white everywhere else. But the growth of the new plumage was still very slow; new white feathers made their appearance in fresh places, and some old ones still grew, but long feathers on the wings and tail did not grow at all.

Jan. 18, the lassitude and ataxia previously described had reappeared. Jan. 19, it would not eat at all. Artificial feeding was resumed. The weight had fallen to 1500 gm. Jan. 18-26, the treatment was interrupted and the cock was fed bread and milk.

During this period of intermission of treatment the plumage grew very much more rapidly, the wing feathers beginning to grow partly white and partly black with large white spots near the tips; whereas during the second period of gland treatment the roots of the young feathers that had started after the first period of the treatment had weakened and were beginning to drop.

Jan. 27, the third period of treatment began. The cock regularly received a twelfth, eighth or quarter of a gland. Feb. 6, it had half a gland, and the next day the symptoms of derangement of gait and incoordination reappeared so that it had to be artificially fed.

Many new white feathers were appearing on the wings. Feb. 8, 10 and 11, it had doses of a twelfth of a gland and appeared better, eating with a good appetite. From Feb. 18-27 it was given in increased doses up to a third or a half of a gland. The most evident effect was excitability, restlessness, muscular tremors, thirst, very loose bowels and much flatulence.

Feb. 28, the cock was again utterly depressed, the feathers moulted considerably, and the weight had decreased noticeably. From this point the thyroid treatment was suspended and the cock recovered and again was pecking, though only from the palm, not from the floor. The feathers continued to drop as at every period of treatment.

March 4, the cock showed a general dark coloring with occasional white feathers. Most of the white plumage was concealed beneath the wings and colored parts. At the same time many other peculiar-

ities were observed; postponed growth and development, an outward appearance which might be called either senile or infantile; a pale comb, half grown; stunted growth; absence of spurs; and bent and knotted legs.

After reaching such a condition the cock recovered a normal condition, but with surprising tardiness. On March 21 there was a great increase in size, and the comb turned red, only at this stage acquiring the characteristic backward fold on to the forehead and sharp dentation. However, the cock still startled and amazed onlookers with its imbecility, strutting about crazily and stumbling over the other fowls and rabbits in the pen. The roosting instinct was absent and it never even tried to crow.

April 28, for the first time it displayed something like a sexual instinct. On May 12, when approaching the hand with the grains in it, it uttered for the first time the cock's characteristic note, the cluck that summons the hens; but it still could not peck one grain at a time, and had to be fed by hand. After this date exact observations could not be continued, but in June the cock began crowing and pairing.

Autopsy, July 20, showed the following conditions. The comb and gills had grown almost to normal size and become a bright scarlet, and the bird had grown strong and increased in weight (2480 gm.). The plumage had become duller than is usual in this variety in spite of very many contour feathers which had grown afresh after the conclusion of the experiment and covered up the white feathers. The tail feathers were just beginning to grow, but very much delayed. The characteristic of the legs remained unchanged.

The limits of space will not permit detail of other observations, but similar experiments left it beyond all doubt what were the specific and essential symptoms. Results such as those illustrated in Figure 1 prove that the different varieties of black fowls are subject to depigmentation (Langshan, Spanish and "Minors").

One point yet remained to be decided: was it only the black pigment that was liable to discoloration under thyroid feeding, or other colors as well? Incidental experiments with other varieties, mainly brown, yellow and grey, tended to indicate that the black was not in this respect an exception among other color pigments. It was decided to settle this question by experimenting on red plumed Rhode Island birds. The details of an experiment on such a bird corroborated our expectations.

Experiment No. 33 was carried out with the assistance of S. A. Azimova-Milietzcoja on a Rhode Island Red hen obtained with its sister and a cock from the great Moscow breeding station of Gorjunov.

Feb. 20-22, 1923, one-quarter horse thyroid gland daily was administered. Feb. 23-26, another quarter gland daily was given. Feb. 26, the hen, when handled, lost many feathers which remained in the observer's hands and easily fell out of their sockets. On

Feb. 28 both the experimental hen and the control had the feathers plucked off the right side of their legs to hasten pigmentary reaction. Feb. 29 to March 3, the treatment was interrupted. The hen moulted heavily, leaving its back absolutely bare; feathers dropped off the entire body. On the back and on the right side of the plucked leg white feathers grew, while red feathers grew on the control hen.

On March 8 a third of a gland was given, and on March 10, 12, 13 and 15 a quarter of a gland. After March 15 the experiment was discontinued, as the discoloration was most pronounced. The control hen, however, did not show a single white spot on the leg or any other part of the body. Figure 2 shows clearly the degree of whiteness attained by the hen under treatment, as compared with the control sister. The stuffed specimens were prepared July 13, 1923.

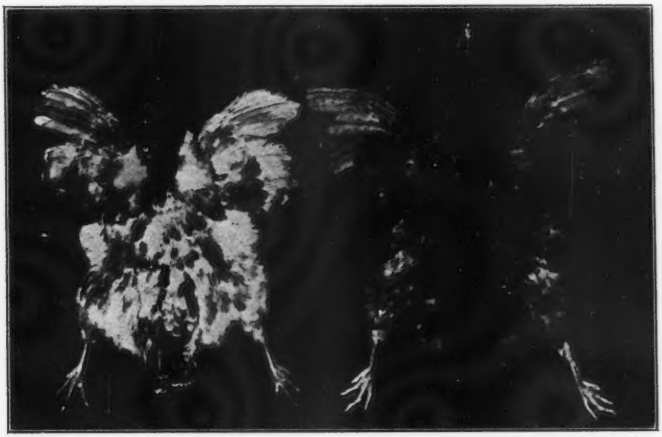

Figure 2. The depigmented Rhode Island hen and her control sister.

Many similar experiments on various fowls, yellow, cream, grey Plymouth Rock (although mostly hybrids), confirm the view that *every pigmentation in fowls is subject to discoloration under thyroid gland treatment,* and apparently this process is faster in colors other than black. However, this latter supposition has not yet been conclusively proved.

To sum up the outcome of these lengthly observations two points may be taken as absolutely demonstrated: that treatment with thyroid gland will provoke premature moulting in fowls, capable of repetition with subsequent growth of white feathers, and a general change in the quantity of the pigment of the new plumage.

But these conclusions also involve a series of new problems bearing on the character of the effect of thyroid gland treatment.

At Ascania and Odessa the experiments were carried out on fowls between July and December, i. e. when fowls normally moult. Also, the doses used up to that time were very large, and beyond doubt exceeded the limits of normal physiological action of the thyroid gland. Therefore two questions remained to be solved. (1) *Would small (physiological) doses of thyroid gland produce analogous results on the moulting and the pigment?* (2) In the experiments reported the natural glands of sheep or oxen mostly were used. With the artificial prepara-

Figure 3. 1-9—Feathers of Langshan cock after thyroid feeding.
10-11—Feathers of control Langshan.
Middle row—Feathers of Rhode Island Red cock.
I and II before, and III-X after, the thyroid feeding.
A and F—Normal feathers of Rhode Island Red hen.
B-E—Depigmented feathers of a hen fed with thyroid.

tions of Poehl such exact and positive results in moulting and discoloration were not obtained and it was thought that these artificial preparations of the gland lacked this specific reaction. In this event, the theory would be confirmed that the hormone of the thyroid gland is not a simple body, but a complex of independent entities. Is such actually the case? *Do derived preparations yield the same result as natural glands?*

From Jan. 26 to Feb. 3 a mongrel black Spanish pullet, weighing 1217 gm., received about 10 gm. of Poehl's thyroidin either in tablets or in powder. In about one month from the beginning of the experiment the head was checkered with white, and soon after white spots also appeared on the wings and thighs. It is remarkable that the dose fixed upon for this experiment failed to produce a state of depression on this fowl; on the contrary, the weight increased to 1420 gm. There was no moulting at first; it began only after prolonged dosage, Feb. 10. This intense moulting lasted about ten days.

In view of this positive result the fowl from Dec. 14 onward was given natural horse gland, and as much as a quarter to a half gland a day. Towards the end of January she had such an abundance of white feathers that from raven-black she had turned into something like a speckled partridge.

The other hen was a cross with a few white and grey feathers on a background of black, of the same age, and weighing 1175 gm. She received the same doses and produced a plentiful white plumage, the white feathers amounting to two or three times the original number. The development in this case proceeded quite similarly to that of the other, both in the production of white feathers and in the commencement of the moulting.

Thus it was evident that the effective substance was present in the Poehl preparation. And further, these results were attained with doses of gland scarcely exceeding the physiological limits. The experiment affected both chickens toward the end of the normal moulting and therefore retarded the production of pigment in the normal growth of the young feathers. It appears that the young plumage is less liable to moulting than the old plumage. This conclusion was borne out by three further experiments which proved that *soon after the normal moulting the plumage is much more firmly attached and only very slightly subject to moulting,* even if very large doses of thyroid gland are administered.

The reversal of the depigmentation. One of the hens that showed a marked depigmentation was kept all the summer after the termination of the experiment in March, 1922. *In the*

autumn after the normal moulting she reassumed her black plumage.

On Dec. 1, 1922, she was again fed on horse gland, an eighth to a half of the gland daily. The feeding was continued until Jan. 12, 1923, with an interval from Dec. 7-22. Moulting began on Dec. 12. On Jan. 13 she died in typical convulsions, but abundantly covered with white feathers.

Neuropathological symptoms. In several other cases than that described in the first protocol special attention was paid to

Figure 4. Spanish hen after a second thyroid feeding.

the neurological effects of thyroid feeding. An outstanding result is general stupidity. Disturbed balance and lack of coordination in the nervous system as a whole is evident. Various aspects of the neurological problem remain for further study. In general the greatest development of neurological symptoms coincided with depression of weight and ischemia and shrinkage of the comb.

Control experiments. As previously stated, during the earlier experiments a considerable number of fowls were fed as controls with large amounts of meat concurrently with the fowls under thyroid treatment. In no case were symptoms observed anything like those seen in hyperthyroidized fowls. This fact raised the question: Does the depigmentation play an independent part in the symptoms as observed or is it merely a change due to the precedent moulting, a sign of a certain weakening of epidermal functions? To answer this, both control fowls and those undergoing treatment were frequently plucked on definite parts of the body, generally the thigh and under the wing. In every case the feathers of the control fowls when they grew afresh were of normal color, while the thyroidized fowls grew great patches of white feathers. It appeared also that the pigment reaction can be obtained with less thyroid than the moulting reaction.

Although already in possession of a whole series of control facts it was thought advisable to check the experiments in yet another way, by using fowls fed on other organs of internal secretion. Adrenal bodies were selected as most readily available and also because there is evidence that they have a direct functional (synergistic) relation to the thyroid gland.

Further, there is the well known fact of the bronzing of the skin in Addison's disease, which is connected with the affection of the cortex of the suprarenals. A posteriori, it might be supposed that if we introduced into the system doses of suprarenal glands far above the normal in quantity we might induce depigmentation of the dermis. The extent to which the suprarenal gland can evoke symptoms similar to those resulting from hyperthyroidism of fowls was therefore investigated. Thus, with the assistance of S. A. Miliezcoja-Azimova suprarenal in doses of one-fourth to a whole gland was administered.

Four fowls, two white and two black, and several controls were used. Suffice to say that with the exception of one case in which gain in weight was less than expected, no effect of the feeding as detected. The experiment was continued by the injection of adrenalin chloride (Parke, Davis & Co.) in doses from 2 to 10 cc. over a period of ten days. No effects were produced that could be related to the specific thyroid action.

SUMMARY AND CONCLUSIONS

1. Thyroid preparations were administered to about sixty fowls. These included dried or fresh glands of sheep, oxen and horses and Poehl's thyroidin. No significant differences in the effects of these preparations were observed.

2. The toxic threshold in birds proved to be much higher than in mammals.

3. The dosages ranged from minimal to fatal.

4. The symptoms of hyperthyroidism demonstrated were increased excitability, polyphagia, polydipsia and nervous disturbances which varied with the doses.

5. The neuropathologic disturbances included incoordination, convulsions and general stupidity.

6. An effect specific to fowls was observed in the plumage. Larger doses caused a marked loss of feathers. These were replaced by others which were completely colorless or white in varying degrees, depending upon dosage.

7. It is concluded that the thyroid gland plays a specific role in the regulation of the growth and moulting of feathers and in their pigmentation.

In conclusion I wish to express my gratitude to Prof. Boris Petrovich Babkin, who, in the troublesome years of 1919-20, afforded me a place and the opportunity of work in his physiological laboratory at Odessa; as an assistant there and working under him, I received valuable guidance and encouragement in my scientific pursuits.

Warm thanks are also due to my brother, Prof. Michael Zavadovsky, with whom I have frequently discussed this work during its progress and after its conclusion.

INCIDENCE OF GOITER AMONG SCHOOL CHILDREN

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Simple goiter, or benign enlargement of the thyroid gland, is of common occurrence in the United States. It is endemic in the entire basin of the Great Lakes and in the Pacific Northwest. King County, Wash., is in a region with large incidence of endemic goiter. The common occurrence of this condition locally will be testified to by any practicing physician, and the layman on the street can readily diagnose cases in abundance as he passes. Over fourteen thousand observations on local University students show an incidence of over twenty-six per cent, while an even more frequent occurrence of thyroid enlargement was noted in an investigation in a few of the public schools. Although decreased incidence of goiter in adults as contrasted with that noted in early life may be established, nevertheless the goiter in the adult, which often develops into the severly toxic type, may have its origin in the simple endemic goiter of childhood.

The endemiology and etiology of simple goiter have long engaged the attention of investigators. Various theories are proposed in this connection. The chemical hypothesis attributes the disturbance to the presence of various chemical agents in the water, such as magnesium, iron salts, calcium salts and iodine. The organic theory postulates the presence of toxin of organic nature in water. McCarrison's well known bacterial theory of the origin of goiter is supported by much evidence. The presence of acute or chronic infection, tonsillar, gastrointestinal, or of other focal origin, is at times considered responsible.

Whatever final conclusions may be arrived at relative to the ultimate cause of goiter, certain indisputable facts as to the control of its occurrence are now at hand. Kimball points out that iodine was used in a treatment of goiter by the ancient Greeks in the form of the ash of burnt sea sponges. Marine and

Lenhart show that in the dog, if a fragment of the thyroid gland no larger than one-sixth of the total normal tissue is allowed to remain in situ, and five-sixths of the gland removed, the fragment will not enlarge if the animal is given sufficient iodine to keep the fragment saturated. If the iodine content of the thyroid gland of animals is deficient in iodine, the young are born with goiters.

The active principle of the thyroid gland was isolated in crystalline form by Kendall in 1916. This substance is a stable compound of iodine. It loses its physiological activity, however, if the iodine is replaced by other halogens. The conclusion is then drawn that iodine is necessary for normal thyroid function. When there is a deficiency of iodine, the thyroid gland enlarges in an endeavor to meet the bodily demands for its normal secretion. Marine and Lenhart state that the iodine content of thyroid gland substance varies inversely with the degree of hyperplasia of the gland.

"Simple goiter is the easiest known disease to prevent" (Marine). This sweeping statement is fully substantiated by the experience of live stock owners in eradicating the disease from stock, and by the clinical results already obtained in various parts of the United States and in Switzerland. The accomplishment of prophylactic treatment of simple goiter centers around the work of Marine and Kimball, carried on in the city of Akron, Ohio. These workers obtained the permission of the School Board of Akron to work in the public schools, and outlined a method of approach which would give them clear cut and definite observations upon which to draw definite conclusions.

One man was chosen to do all the physical examinations, so that the observations might be consistent, and certain criteria were outlined which were arbitrary, but served as a guide to aid in classification. These criteria were as follows:

A thyroid gland was considered normal:

(a) Which was not visible, as a bulging across the trachea;

(b) Which had a barely detectable band of thyroid tissue across the trachea, on palpation;

(c) In which there was absence of a well-defined thyroglossal stalk (so called pyramidal process).

Enlarged thyroids were grouped in three classes:

1. (a) Visible bulging of the skin over the thyroid isthmus;
   (b) A widened or thickened isthmial band or mass on palpation. (If the isthmus cannot be seen or felt it can be felt by having the child swallow while the finger or thumb is held against the trachea just below the cricoid cartilage.)
2. Moderate enlargement consisting of:
   (a) Gross deformity;
   (b) Bulging of the neck from the enlarged lobe;
   (c) Marked bulging of the skin anterior to the enlarged isthmus.
3. Marked enlargement consisting of those cases with excessive deformity.

The results obtained by these men, in brief, were as follows:

Of 2090 pupils taking iodine, 5 developed enlargement of the thyroid gland;

Of 2305 not taking iodine, 495 developed thyroid enlargement;

In 1182 pupils with enlargement of the thyroid gland at first examination, who took iodine, 773 thyroids were decreased in size;

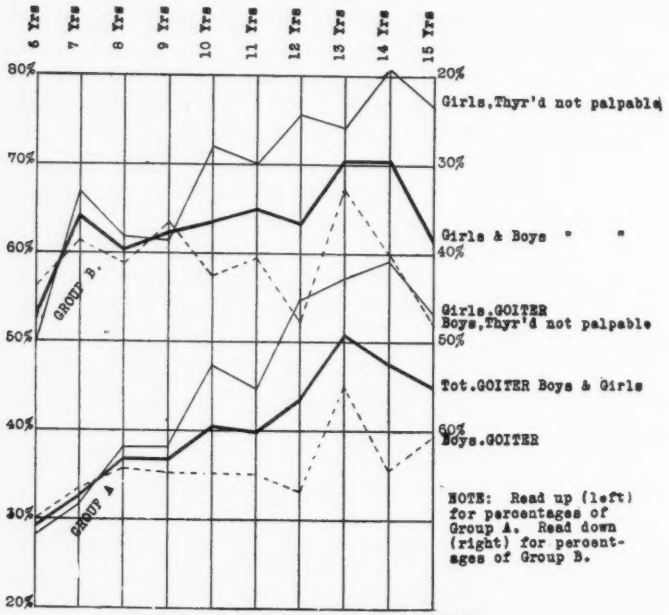
In 1048 pupils with enlarged thyroid glands at first examination, who did not take iodine, only 145 decreased in size.

The experience of these men indicates that goiter is found six times as frequently in girls as it is in boys, and that the best ages for prophylactic treatment are from 11 to 17 years of age. A more recent survey in Grand Rapids, Michigan, covering over twenty-six thousand school children, does not bear out this ratio if thyroid enlargements of minor degree are included. The slight enlargements are much more common in boys than earlier statistics indicate, but have apparently been largely overlooked. This last observation is borne out in the King County District, herewith reported.

In 1918 goiter prevention by means of iodine administration was undertaken in Switzerland. At that time in one of

the Zurich schools one hundred per cent of the children were goiterous. A few milligrams of iodine was given weekly throughout the school year, with a resultant marked reduction in the incidence of goiter. In the Canton of St. Gall, in January, 1918, an incidence of 87.6% was reduced to one of 13.1% in January, 1922. On the basis of these results, prophylactic treatment of goiter is being extended throughout Switzerland.

With the above facts in mind, a committee appointed by the King County Medical Society, and composed of the signers of



FINDINGS OF 3160 EXAMINATIONS FOR GOITER AMONG GRADE SCHOOL CHILDREN (1506 GIRLS AND 1654 BOYS)

this report, undertook a survey of the school children of King County to determine accurately the incidence of goiter. One school was chosen, and after having studied carefully the criteria of classification as outlined by Marine and Kimball, the members of this committee spent some time in satisfying themselves that each man had a clear understanding of the interpretation

of the facts in hand. It did not take long to realize that there were many children in whom the isthmus of the thyroid gland was readily palpated and was from ¾ to 2 centimeters in breadth. In addition to this there was another group of children in whom the thyroid enlargement was so prominent that one could see bulging of the neck, and it was palpated so readily that it could easily be demonstrated to the teacher. The first group the committee decided to classify simply as palpable glands, while the second group was designated as definite enlargement of one, two or three degrees. Some three thousand children were examined according to these standards, and the results were submitted for investigation.

Pupils examined	3,160
Boys examined	1,654
Girls examined	1,506
Boys with goiter 1 and 2	588
Girls with goiter 1 and 2	655
Per cent among boys	35.5
Per eent among girls	43.4
Total percentage among boys and girls	39.3

TABLE 1

Age	No.	NOT PALPABLE		PALPABLE		NO. 1		NO. 2 AND 3		TOTAL GOITER	
		Neg.	%	No.	%	No.	%	No.	%	No.	%
6	319	150	47.00	75	23.8	90	28.2	3	0.94	93	29.14
7	325	117	36.00	102	31.38	104	32.00	2	0.6	106	32.6
8	395	157	39.74	92	23.29	138	34.93	8	2.02	146	36.95
9	420	158	37.62	108	25.71	147	35.00	7	1.66	154	36.66
10	406	148	36.45	94	23.15	158	38.91	6	1.48	164	40.39
11	385	135	35.06	96	24.93	144	37.4	10	2.59	154	39.99
12	344	126	36.62	69	20.05	136	39.53	13	3.77	149	43.30
13	313	93	29.71	61	19.48	137	43.77	22	7.02	159	50.79
14	175	52	29.70	40	22.85	68	38.85	15	8.57	83	47.42
15	78	30	38.46	13	16.66	30	38.46	5	6.41	35	44.87
TOTAL	3160	1166	36.9	751	23.76	1152	36.45	91	2.88	1243	39.3

Findings of 3,160 Examinations for Goiter Among Grade School Children.

The findings presented in the chart indicate much earlier age incidence of goiter among school children than has hereto-

fore been noted. The relative incidence among boys as contrasted with girls is likewise much greater than earlier reported. This corresponds with the findings in Michigan. An apparent

TABLE 2

Age	No	THYROID NOT PALPABLE		THYROID PALPABLE		GOITER NO. 1		GOITER NO. 2 AND 3		TOTAL GOITER	
		No.	%	No.	%	No.	%	No.	%	No.	%
6	153	67	43.8	40	26.1	46	30.0	....	.....	46	30.0
7	163	63	38.88	45	27.7	53	32.7	1	0.61	54	33.31
8	212	87	41.0	49	23.1	72	33.9	4	1.88	76	35.78
9	216	79	36.57	61	28.23	73	33.79	3	1.38	76	35.17
10	235	100	43.45	52	22.7	82	34.9	1	0.42	83	35.32
11	191	77	40.31	47	24.6	63	32.98	4	2.09	67	35.07
12	180	86	47.7	35	19.4	56	31.6	3	1.66	59	33.26
13	170	56	32.9	37	21.71	71	41.76	6	3.52	77	45.28
14	87	35	40.23	21	24.13	26	29.88	5	5.74	31	35.62
15	48	23	47.91	6	12.50	18	37.15	1	2.08	19	39.58
TOTAL	1654	673	40.6	393	23.7	560	33.85	28	1.69	588	35.5

Findings of 1,654 Examinations for Goiter Among Grade School Boys.

TABLE 3

Age	No.	THYROID NOT PALPABLE		THYROID PALPABLE		GOITER NO. 1		GOITER NO. 2 AND 3		TOTAL GOITER	
		No.	%	No.	%	No.	%	No.	%	No.	%
6	166	83	50.00	36	21.68	44	26.5	3	1.8	47	28.3
7	163	54	33.12	57	34.97	51	31.29	1	0.61	52	31.9
8	183	70	38.24	43	23.49	66	36.06	4	2.19	70	38.25
9	204	79	38.72	47	23.03	74	36.27	4	1.96	78	38.23
10	171	48	28.07	42	24.56	76	44.44	5	2.92	81	47.36
11	194	58	29.89	49	25.26	81	41.75	6	3.09	87	44.84
12	164	40	24.39	34	20.73	80	48.78	10	6.09	90	54.87
13	143	37	25.87	24	16.78	66	46.15	16	11.19	82	57.34
14	88	17	19.31	19	21.59	42	47.95	10	11.3	52	59.25
15	30	7	23.33	7	23.33	12	40.0	4	13.33	16	53.33
TOTAL	1506	493	32.7	358	23.7	592	39.3	63	4.1	655	43.4

Findings of 1,506 Examinations for Goiter Among Grade School Girls.

drop in the percentage of enlarged thyroid glands at the age of 14 in boys, and 15 in girls, is not so reliable as the findings plot-

ted up to those ages, since relatively few examinations of children 14 and 15 years of age were made.

BIBLIOGRAPHY

1. Guilder, Ruth P.: Incidence of goiter among college students. Ann. Clin. Med. (Balt.), 1923, **1**, 248.
2. Reed, T., & Clay, H. T.: A survey of thyroid enlargement among the school children of Grand Rapids. J. Mich. M. Soc. (Grand Rapids), 1923, **22**, 323.
3. Watt, C. H.: Simple goiter—its local prevalence. J. Med. Ass. Georgia (Augusta), 1923, **12**, 177.
4. Pearce, N. O.: Incidence and prevention of thyroid disease among children. J. Lancet, 1923, **43**, 157.
5. Hall, D. C.: Prevalence of goiter in the Northwest. Northwest Med. (Seattle), **6**, 189.
6. Hall, D. C.: Prevalence and distribution of goiter in Washington. Ibid., 371.
7. Schlesinger, E.: Ztschr. f. Kinderh. (Berl.), 1920, **27**, 207; abst., J. Am. M. Ass. (Chicago), 1921, **76**, 1376.
8. Kraeuter, J.: München. med. Wchnschr., 1922, **69**, 47; abst., J. Am. M. Ass. (Chicago), 1922, **78**, No. 4.
9. Skolstad, S.: Norsk Mag. f. Laegevidensk. (Christiania), 1921, **82**, 729; abst., J. Am. M. Ass. (Chicago), 1921, **77**, 1613.

THE EFFECT OF PITUITARY PREPARATIONS ON THE NITROGEN METABOLISM*

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The influence of the glands of internal secretion on metabolism is so firmly established that we were led, in the course of another investigation, to administer various pituitary preparations to patients on a constant protein intake to see if any effect on the nitrogenous output could be demonstrated from preparations which have been shown to exert a profound influence on growth and water metabolism.

Various attacks have been made upon this problem, but the results have been conflicting (1, 2). In these experiments human subjects were used. With three exceptions all were physically normal adults. Of these three, two were Mongolian idiots and one was a cretin, but these also were of adult calendar age. These three patients were studied at an earlier period and blood determinations were not carried out. The methods used were those of Folin (3) for both blood and urine except for the uric acid determinations which were done by Benedict's method (4). Complete nitrogen partition was determined daily on the urine. The patients studied were kept in a small ward and their activity was limited to walking about the ward. All the food served to them was cooked in a small diet kitchen on the ward and carefully weighed by a nurse especially trained for this work.†

The drugs used were commercial extracts bought in the open market. The doses were as follows: "Pituitrin (Surgical)" 1.0 cc., "Posterior Pituitary" 20 mgms, "Anterior Pituitary" 324 mgs., "Whole Pituitary" 324 mgms. These doses were given three times a day after meals. The results are

*From the Laboratory of Internal Medicine in the Boston Psychopathic Hospital.

This paper is No. 42 of a series of studies in metabolism from the Harvard Medical School and allied hospitals. The expenses of this investigation have been defrayed in part by a grant from the Proctor Fund of the Harvard Medical School for the Study of Chronic Disease.

†We wish to acknowledge the invaluable assistance of Miss M. F. Nelson, R. N., in preparing and calculating the diets and acting as head nurse of the ward.

shown in the accompanying tables. Table 1 shows the effect of anterior and posterior lobe administration to normal subjects. The blood figures show no constant change in any of the nitrogenous constituents, though earlier studies (5) with the methods then available seemed to show an increase in the blood uric acid after administration of desiccated pituitary. Similarly no constant change can be demonstrated in the nitrogen metabolism as shown in the output of urinary nitrogen.

The experiments with Pituitrin and whole gland (Tables 2 and 3) likewise show no demonstrable effects on the nitrogen metabolism in these experiments. It is to be especially noted that no significant variation in the nitrogen partition occurred in either blood or urine.

SUMMARY

No effect on the urinary nitrogen excretion or non-protein nitrogen of the blood was observed in these experiments as a result of the administration of either pituitrin (intramuscularly), dried anterior lobe, dried posterior lobe or dried whole gland pituitary (by mouth) to patients on a constant diet.

BIBLIOGRAPHY

1. Malcolm, J.: J. Physiol. (Lond.), 1903, **30**, 270.
2. Schafer, E. A.: Quart. J. Exper. Physiol. (Lond.), 1912, **5**, 203.
3. Folin, O.: A laboratory manual of biological chemistry. D. Appleton & Co., N. Y., 1922.
4. Benedict, S. R.: J. Biol. Chem. (Balt.), 1922, **51**, 187.
5. Hammett, F. S., Patten, C. A., & Suitsu, J. N.: Am. J. Physiol. (Balt.), 1920, **51**, 588.

(Tables will be found on following pages.—Publishers.)

TABLE 1

Table 1. Experiments showing the effect of surgical pituitrin (1 cc. t. i. d. intramuscularly) on blood and urinary nitrogen. The drug was administered on the first three days of the experiment, so that the anaylses of days Nos. 2, 3 and 4 show the effects during the exhibition of the drug. The first day is free from any drug influence, being the last day of a control period.

TABLE 1

Subject	Day of experiment	URINE						BLOOD					
		Total nitrogen	Urea nitrogen	Ammonia nitrogen	Uric acid	Creatinine	Rest nitrogen	Non-protein nitrogen	Urea nitrogen	Amino acid nitrogen	Creatinine	Uric acid	Rest nitrogen
C VIII	1	6.0	4.5	.4	.3	1.3	.4	27.3	15.2	6.8	1.4	4.5	3.3
	2	5.0	3.9	.4	.3	1.1	.3	25.6	14.3	6.7	1.3	3.8	3.9
	3	5.1	3.9	.4	.3	1.4	.3	29.1	13.1	6.0	1.3	4.2	8.2
	4	6.2	5.0	.4	.3	1.5	.2	33.1	18.8	7.4	1.2	3.6	5.3
	5	6.5	5.3	.4	.3	1.3	.2						
	6	5.0	4.0	.3	.3	1.3	.1						
W XI	1	7.3	5.4	.5	.4	1.5	.8	25.8	10.8	5.4	1.4	4.1	7.8
	2	5.7	4.3	.3	.3	1.6	.4	27.2	12.6	6.0	1.2	3.4	7.1
	3	6.9	5.5	.3	.3	1.5	.5	24.5	12.3	5.4	1.2	3.7	5.1
	4	7.7	6.3	.4	.3	1.7	.2	26.3	15.0	6.4	1.3	4.6	2.9
	5	7.6	6.4	.4	.3	1.4	.2						
	6	6.8	5.1	.4	.3	1.5	.7						
P XIII	1	8.5	6.6	.7	.4	1.5	.6	25.0	13.1	5.9	1.4	3.5	4.3
	2	7.7	5.8	.4	.3	1.1	1.0	24.5	13.0	5.7	1.4	3.4	4.1
	3	7.7	5.5	.6	.3	1.1	1.0	23.4	14.1	5.9	1.3	3.3	1.9
	4	8.1	6.3	.7	.4	1.5	.5	26.9	12.5	5.7	1.1	3.4	7.2
	5	7.2	5.9	.5	.3	1.3	.3						
	6	8.7	6.3	.5	.3	1.2	1.3						
Ha 21 (Mongolian idiot)	1	4.5	3.4	.4	.3	.9	.3						
	2	5.7	3.5	.4	.3	1.1	1.7						
	3	4.8	3.4	.4	.4	1.2	.5						
	4	4.0	3.0	.3	.3	.8	.3						
	5	4.6	3.4	.4	.4	1.1	.3						
	6	5.5	4.0	.3	.4	1.2	.7						
Da 21 (Cretin)	1	4.1	2.8	.3	.4	.8	.6						
	2	4.0	1.5	.2	.3	.7	2.0						
	3	3.9	2.5	.3	.3	.7	.8						
	4	2.5	1.8	.2	.2	.6	.2						
	5	3.2	2.7	.2	.3	.7	.....						
	6	4.0	2.5	.3	.3	.7	.9						
Sp. 21	1	7.6	5.6	.4	.5	1.7	.8						
	2	8.0	3.7	.5	.5	1.8	3.0						
	3	7.5	5.5	.5	.4	1.6	.9						
	4	7.7	5.8	.5	.4	1.8	1.0						
	5	7.1	5.8	.4	.4	1.2	.4						
	6	7.8	5.1	.5	.5	1.9	1.4						

TABLE 2

Subject	Day of experiment	URINE						BLOOD						Drug
		Total nitrogen	Urea nitrogen	Ammonia nitrogen	Uric acid	Creatinine	Rest nitrogen	Non-protein nitrogen	Urea nitrogen	Amino acid nitrogen	Creatinine	Uric acid	Rest nitrogen	
G IX	1	4.8	3.4	.4	.4	1.1	.1	25.0	7.7	5.8	1.3	3.2	9.9	
	2	4.7	3.1	1.0	.3	1.1	.1	26.0	6.3	5.4	1.2	3.7	11.7	Anterior pituitary 1,0 gram t.i.d.p.c.
	3	4.2	2.7	.5	.4	1.1	.5	25.2	8.0	5.2	1.2	3.2	10.4	
	4	3.8	2.7	.5	.3	1.0	.1	26.1	8.6	4.9	1.1	2.8	11.3	
	5	5.1	3.3	.9	.4	1.0	.3							
	6	4.5	2.8	.4	.4	1.1	.8							
P X	1	6.3	4.5	.5	.3	1.4	.7	26.1	6.2	5.2	1.3	3.5	13.1	
	2	5.7	4.1	.9	.3	1.3	.1	25.0	7.0	4.9	1.3	3.7	11.4	Anterior pituitary 1,0 gram t.i.d.p.c.
	3	6.7	5.2	.4	.3	1.4	.5	21.4	8.0	4.7	1.1	3.8	7.0	
	4	4.3	3.3	.3	.2	1.4	.1	24.2	5.5	4.8	1.1	3.6	12.3	
	5	9.2	5.9	2.1	.4	1.9	.3							
	6	6.3	4.4	.3	.3	1.3	1.0							
J XII	1	8.0	5.2	.4	.4	1.8	1.6	25.4	5.7	6.0	1.5	4.1	11.8	
	2	7.0	4.8	.3	.4	1.6	1.2	25.4	6.3	5.2	1.3	4.2	12.0	Anterior pituitary 1,0 gram t.i.d.p.c.
	3	7.3	5.4	.7	.4	1.4	.5	25.2	7.1	5.1	1.3	4.0	11.2	
	4	5.6	4.1	.5	.3	1.3	.4	25.9	8.6	5.4	1.2	3.6	10.3	
	5	8.1	5.7	.6	.5	1.8	.9							
	6	5.9	4.3	.7	.3	1.5	.3							
P X	1	6.4	4.9	.2	.3	1.2	.6	23.1	10.1	5.1	1.1	4.2	6.1	
	2	6.1	5.2	.2	.3	1.1	.2	20.1	9.9	5.2	1.1	3.7	3.4	Posterior pituitary 20 mgms. t.i.d.p.c.
	3	4.1	2.9	.1	.3	.9	.7	21.5	11.0	5.1	1.2	3.6	3.4	
	4	5.7	4.5	.3	.3	1.3	.3	20.9	11.0	5.7	1.3	4.4	7.2	
	5	4.6	3.5	.1	.2	.8	.6							
	6	8.3	6.0	1.1	.3	1.6	.5							
J XII	1	6.2	4.4	.4	.3	1.4	.8	23.1	8.5	8.8	1.1	3.3	4.3	
	2	5.2	3.9	.2	.3	.9	.6	21.5	9.9	5.4	1.2	3.7	4.6	Posterior pituitary 20 mgms. t.i.d.p.c.
	3	4.1	2.7	.3	.3	1.3	.5	26.8	9.4	5.9	1.3	3.9	9.7	
	4	2.2	1.8	.1	.1	.5	.1	22.1	10.6	5.1	1.2	3.2	4.9	
	5	7.6	6.0	.5	.3	1.7	.4							
	6	7.6	5.5	.5	.2	1.4	1.0							

Shows experiments with anterior and posterior lobe administration. Arrangement as in Table 1.

TABLE 3

Subject	Day of experiment	Total nitrogen	Urea nitrogen	Ammonia nitrogen	Uric Acid	Creatinine	Rest nitrogen
Da 21 Cretin	1	3.2	2.0	.2	.3	.7	.7
	2	2.8	2.1	.2	.2	.6	.1
	3	.8	.6	.1	.2	.2	...
	4	4.1	2.8	.3	.4	.8	.6
Sp 21 Psychoneurosis	1	8.6	6.2	.4	.5	1.8	1.2
	2	8.1	6.0	1.0	.5	1.8	.3
	3	8.6	6.7	.4	.6	1.7	.7
	4	7.6	5.6	.4	.5	1.7	.9
Ha 21 Mongolian	1	5.7	4.7	.3	.5	1.1	.2
	2	5.2	3.8	.5	.4	1.1	.4
	3	3.8	2.8	.4	.4	.8	.2
	4	5.7	3.4	.4	.3	.9	1.5
Ca 21 Mongolian	1	6.1	4.4	.2	.5	1.2	.9
	2	5.9	4.7	.2	.4	1.2	.5
	3	5.2	3.9	.3	.4	1.0	.5
	4	6.6	5.1	.3	.5	1.0	.8

Table 3 shows effect on urinary nitrogen output of whole desiccated pituitary (1 gm. t. i. d. p. c.) administered for two days. The second and third days of each experiment correspond to the exhibition of the drug.

Book Reviews

THE INTERNAL SECRETION OF THE SEX GLANDS. Alexander Lipschütz, 1924. Williams & Wilkins Co., Balt. Pp. 513.

Professor Lipschütz has given us in his new book one of the most comprehensive discussion of the endocrine function of the sex glands that has yet appeared. The general theme of the work as stated in the opening chapter is this: to what extent is it possible to show that the ontogenetic development of the sexual characters is influenced by the sexual glands, and that the further persistence of these characters depends on the presence of the sexual glands? In formulating his answer to this question he considers in turn the evidence that has accumulated from experiments on castration, on the transplantation of ovaries and testes, and on the feeding of sexual glands or the injection of their extracts. In each case a concise statement of the results obtained by the more important investigators in the field is first given, followed by an able consideration of the theoretical significance of these results. By this line of reasoning Lipschütz proves the existence of the testicular and ovarian hormones. He then turns his attention to the consideration of the parts of the sex glands concerned in the elaboration of these hormones. After a careful weighing of the available evidence the conclusion reached in regard to the testes is that in the mammal "the interstitial cells are a necessary part of the endocrine apparatus," while "no proof exists of a direct hormonic action by the cells of Sertoli or by the other constituents of the walls of the tubules independently of the interstitial cells." The author is inclined, however, to believe that while the generative cells are not concerned directly in the elaboration of a hormone, still the process of spermatogenesis or some stage in the process is connected with the transformation of the interstitial cells into an active endocrine apparatus. In the case of the ovary the author concludes that it is highly probable that in the mammal the internal secretion is elaborated partly by the membrana granulosa, and partly by the cells of the theca interna, and that these cells originate from follicles undergoing atresia or from ripe follicles rupturing and transforming themselves into corpora lutea.

There is a chapter on the isolation of the sexual hormones and another in which the author shows that there is little or no

evidence to support the view that the prostate, seminal vesicle, or genital passages are concerned in the elaboration of a hormone although it is probable that the secretions of these parts of the genital apparatus are of great importance to the vitality of the spermatozoa. This is followed by an interesting discussion of the various types of hermaphroditism, eunuchoidism and sexual precocity. The chapter on the sexual hormones and morphogenesis should be of especial interest to geneticists, for in it Lipschütz discusses at some length the problem of sex determination and even succeeds, to a certain extent, in harmonizing his theory of the indifferent character of the soma with the existence of sex chromosomes. The final chapter deals with the problem of rejuvenation and in it the author attempts to show to what extent our knowledge of the sexual hormones may be of importance in the practice of medicine.

The book should have a wide appeal, as it contains material of almost universal interest. All biologists and medical men will find a wealth of valuable material in it, while even the layman without biological training will find much of the book interesting and understandable.—F. A. Hitchcock.

LES SYNDROMES HYPOPHYSAIRES ET EPIPHYSAIRES EN CLINIQUE INFANTILE. Pierre Lereboullet, 1924. J. B. Baillière et Fils, Paris. Pp. 135.

The writer reviews the literature on the experimental physio-pathology of the hypophysis and epiphysis and correlates the findings with the syndromes and morphological changes presented in clinical cases of infantilism. The relation of the hypophysis to osseous dystrophies, glycosuria, polyuria, diabetes insipidus and the adiposogenital syndrome, in young persons, is discussed, together with treatments. The monograph also includes a report of the relation of the epiphysis to precocious puberty, and a discussion of treatments (organotherapy, radiotherapy, and surgery).—M. O. Lee.

PREPARATION OF SCIENTIFIC AND TECHNICAL PAPERS. S. F. Trelease & Emma S. Yule, 1925. Williams & Wilkins Co., Balt. Pp. 113.

The editorial policy of this journal is to restrict this department to review of publications pertaining technically to endocrinology. The excellence and timeliness as well as the need for this little book by Trelease and Yule, however, seem to justify a departure from custom. It is a book that could profitably be read by the great majority of contributors to current scientific literature. It has been evolved, not from the authors' inner conscious-

ness, but from years of experience in which it has been placed as a guide in the hands of technical students. The reviewer upon first reading the book began to mark special passages for comment, but so many admirable things were encountered that the attempt was given up. The outstanding features are a clear, concise presentation of the methods of effective organization of material, a discussion of points of usage frequently overlooked, and an enlightening description of the technic of transforming a manuscript into a printed article. The book is as readable as it is informing.—R. G. H.

Abstract Department

The effect of administering adrenal cortex to young guinea pigs (Primi risultati di ricerche sperimentali sugli effetti della somministrazione di corticale surrenale sull' accrescimento somatico di giovani cavie). Castaldi (L.), Rendic. d. R. Accad. d. Lincei, 1924, **33** (I Sem.), 94-96.

The addition to the ordinary diet of young guinea pigs of 3 to 10 c. per kilo of a dry extract of cortex of suprarenal glands causes a considerable increase in their somatic development. In comparison to untreated controls the animals are heavier and fatter and their skeleton is bigger; the hair reaches an unusual length, particularly in females. If the same extract is administered to pregnant animals the young are larger than those of controls. The administration of the extract prolonged for months does not give rise to toxic or anaphylactic phenomena.—Physiol. Abst., **9**, 543.

The effect of double adrenalectomy on the development of rickets in rats. Hess (A. F.) & Jaffe (H. L.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1924, **22**, 103.

On a defective diet controls and completely adrenalectomized rats developed rickets to the same degree and at the same time. The authors concluded, therefore, that the functional activity of the adrenals is not an essential or an important factor in the pathogenesis or cure of rickets.—J. C. D.

Measurements on the cortical cells of the human adrenal (Messungen an der Zellen der menschlichen Nebennierenrinde). Kolliner (Martha), Ztscher. f. Anat. u. Entwcklngsgesch. (Berl.), 1924, **70**, 321-335.

This report includes a tabulation of measurements on the size of whole cells and nuclei and shows the relation of the two in 29 human subjects, from a 6 cm. fetus to 49 years of age, and in 2 apes. There is surprisingly little change from the fourth fetal month to the adult stage. Literature is cited.—A. T. R.

The relation of adrenalin to the action of insulin upon the blood sugar content. Mueller (E. F.), Lewi (M. J.) & Myers (C. N.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 142-146.

Nine rabbits were tested for their reaction to adrenalin and then for their reaction to insulin. These same rabbits were then injected with both substances.

It was concluded that adrenalin and insulin, administered to the same animal, do not eliminate their mutual actions. In some instances, adrenalin injections made simultaneously with the administration of insulin increase the action of insulin by lowering the blood sugar content more than usual. In some instances, the action of insulin is only slightly diminished in the first tests (2 hours after administration), while the findings after 4 hours manifest an increase in the insulin action, usually observed at that period. It has been demonstrated that (in more than 70% of the cases examined) the insulin effect is generally not eliminated by adrenalin, but is sometimes enlarged. The reasons for these findings have hitherto not been discovered. They may be based upon an action of the involuntary nervous system.—J. C. D.

Studies in Addison's disease. Rowntree (L. G.), J. Am. M. Ass. (Chicago), 1925, **84**, 327-335.

From the analysis made by Rowntree of forty-seven cases of Addison's disease no new facts are definitely established, but, despite the lack of pathologic and bacteriologic evidence, it is impossible to exclude a casual relationship between influenza and Addison's disease, even though it may not be direct. The most accurate data in this study relates to the last twenty-one cases. Thirteen of the patients in this series are dead, the average duration of the disease being sixteen and one-half months. The shortest duration was six weeks, and the longest definite history three and one-half years. Asthenia and pigmentation were present in every case, though in varying degrees. These two symptoms and hypotension were utilized as criteria in making the diagnosis. Gastro-intestinal complaints of one kind or another were present in practically all cases. Anorexia, nausea and vomiting were common, and in all probability were directly responsible for the loss of weight. Of the other gastro-intestinal symptoms, constipation is common, but is often interrupted by marked diarrhea for two or three days. Belching and bloating are also present at times. Pain is not usually described as a symptom of Addison's disease, but a considerable number of patients complained of vague, dull, deep aching pain in the epigastrium, lumbar region or flanks. This may be unilateral or bilateral, and possibly may be suprarenal in origin. Dyspnea, collapse and syncope are probably related to the feeble cardiac action and to the low blood pressure. Shock, or a condition closely

resembling it, has been observed in several cases. The patient is usually conscious, has a low temperature and an extremely low blood pressure, and the flesh feels cold to touch. There may be blood concentration, as evidenced by decreased water content in the blood, and increased difficulty in obtaining venous blood. The blood sugar of one patient, during the shock period, was 0.045 per cent. The pulse rate was between 70 and 100, and weak and compressible, but regular. The heart action was feeble usually, and the apex beat difficult to locate. On auscultation, the sounds were uniformly distant and feeble, and could be heard somewhat better with the ear than with the stethoscope. The respirations were extremely interesting in some cases, especially during the shock-like periods. In one case, they were markedly decreased, nine each minute, irregular in character and interrupted by frequent sighs. Interesting tracings were obtained in two cases. In one, a pneumographic tracing was taken and proved to be similar or identical to the tracing of Biot and to those published later by Conner. The tracing on the second case was somewhat similar, but not identical. So far as Rowntree is aware, these are the only instances recorded of this type of breathing in cases other than those in which there is meningitis or other intracranial lesions. In both cases, moderate acidosis was present. The first patient has improved markedly under treatment. The second responded slightly at first, but nausea and vomiting with extreme hypotension and asthenia continued until death. No suggestion of meningitis existed in either case. The laboratory studies may be summarized briefly. The urine was approximately normal and consistently sugar free. Water tests indicated poor excretion. The fasting blood sugar determined on admission was below normal in nine cases. Gastric contents were studied in nine of the twenty-one cases. In five of these, achlorhydria was present. The total and free acids were low in every instance. Roentgen-ray examination of the chest disclosed evidences of tuberculosis in four cases. Basal metabolism tests were carried out in thirteen cases, eight falling within normal limits. In this group of cases, anemia was infrequent, although a cardinal symptom according to Addison. Differential counts were made in fourteen cases, nine showing a definite lymphocytosis, reaching 50 per cent or more in four cases. The polymorphonuclear cells were decreased proportionately. In two cases tested, hepatic function was undisturbed. Necropsies were obtained in eight cases, and the pathologic involvement of the suprarenals and kidneys was confirmed at operation in another instance. It is rather significant that of the nine cases coming to necropsy, tuberculous lesions were found in eight; in the other case, the process was one of high grade

atrophy. The treatment employed by Rowntree was the so-called Muirhead regimen. The principle of the treatment is the frequent administration of epinephrin hypodermically and by rectum, and of whole gland or suprarenal cortex by mouth to the point of tolerance. This involves the determination of tolerance, which varies widely in each individual case. Once established, it becomes an index to dosage, although the tolerance of the same patient may also vary somewhat from time to time. Other therapeutic factors, such as rest, exercise, diet, outdoor life and sunshine, merit consideration. During the advanced stage and especially during shock, rest in bed should be absolute, and artificial heat is indicated. In stronger patients, moderate exercise, fresh air and sunshine are desirable. Because of the low level of the blood sugar, the diet should be rich in carbohydrates, with feedings at regular and frequent intervals. Long periods of fasting result in exacerbation of weakness; consequently, fruit juices and milk are advocated between meals, and during the night one serving of milk or fruit juice. A small dose of epinephrin is given by proctoclysis during the early morning hours to patients extremely ill. The results of treatment depend to a certain extent on the degree of tolerance which, inexplicably, varies greatly. Patients in the earlier stages, as a rule, tolerate large doses of epinephrin, from 5 to 10 minims (0.3 to 0.6 cc.) or even 15 minims (0.9 cc.), three times a day, hypodermically; from 5 to 10 minims rectally, and from 5 to 10 grains (0.3 to 0.65 gm.) of whole gland or cortex by mouth three times a day. Of the twelve patients on the Muirhead regimen, five are dead and seven living. Notable results were obtained in five instances. Three of these patients are living, are in excellent health, in view of the circumstances, and are continuing treatment after the lapse of from twenty to twenty-six months. The two other patients continue to improve after thirteen and nineteen months, respectively. Emphasis is placed by Rowntree on the improvement accruing under forced organotherapy. The results have exceeded expectations in several instances. On the other hand, despite most thoughtful and continuous efforts, five of the twelve patients died under treatment. The prognosis in Addison's disease is extremely grave. At best, the treatment can only combat functional insufficiency of the suprarenal glands. The treatment probably exerts no influence on the fundamental pathologic processes underlying the addisonian manifestations. Rowntree is of the opinion that since nothing better is available, the Muirhead treatment should be given a fair trial in every case of Addison's disease, care being exercised, however, to see that the patient's individual tolerance is determined and given due consideration, and that simul-

taneously every measure is utilized in combating the associated symptoms and the underlying pathologic process.—A. M. A.

The influence of compounds of known structure on the development of tadpoles (Fortgesetzte Studien über die Beeinflussung der Entwicklung von Kaulquappen durch Verbindungen mit bekannter Struktur). Abderhalden (E.), Arch. f. d. ges. Physiol. (Berl.), 1924, **206**, 467-472.

Growth and metamorphosis are influenced by a single dose of 0.0015 gm. 3-5-diiodotyrosine in 100 cc. water. Hydroxytryptophane accelerates tadpole metamorphosis in similar fashion to diiodotyrosine and **thyroid.** Iodized, this compound is more active. **Insulin** inhibits growth and metamorphosis, and in not too small doses is harmful, frequently producing edema and death.—A. T. C.

Insulin and adrenin action on animals on different diets (Studien über den Einfluss der Ernährung auf die Wirkung bestimmter Inkretstoffe. II, III. Insulin und Adrenalinwirkung bei verschiedenartig arnährten Tieren). Abderhalden (E.) & Wertheimer (E.), Arch. f. d. ges. Physiol. (Berl.), 1924, **205**, 547-558; 559-570.

Rats on a carbohydrate-free diet react less to insulin than rats on rich carbohydrate diet, but give with adrenin more marked hyperglycemia, though no increase in gas-exchange. Rabbits on acid diet (oats) react less to insulin than others on alkaline diet (green food), but give more marked hyperglycemia with adrenin; their alkali reserve is less than that of animals on green food.

—A. T. C.

Influence of diet on the action of certain internal secretions. IV (Studien über den Einfluss der Ernährung auf die Wirkung bestimmter Inkretstoffe). Abderhalden (E.) & Wertheimer (E.), Arch. f. d. ges. Physiol. (Berl.), 1924, **206**, 451-459.

Combined **adrenin** and **insulin** injection into rabbits shows the adrenin effect with animals on acid diet, and the insulin effect with animals on alkaline diet.—A. T. C.

Lipoids in the adrenals and gonads of rabbits (Lipoidbefunde in Nebennieren und Keimdrüsen beim Kaninchen). Bär (R.) & Jaffé (R.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 321-328.

In the adrenal cortex and in the gonads are found regularly phosphatides, cerebrosides and glycerinesters. Cholesterinesters and cholesterin-fatty acid mixtures are found only occasionally and then usually in small quantities. In the adrenals of castrated animals there is considerable fatty acid and soap, probably due to

degeneration of the adrenal cortex. In 2 rabbits fed on cholesterin the adrenals and **ovaries** contained large quantities of cholesterinesters but no phosphatides and cerebrosides. This is regarded as evidence that the lipoids are not secretion products but are merely stored in the cells.—A. T. R.

Absorption of sugar by the isolated heart in the different forms of endocrine insufficiency. Kopelansky (D. S.). Pub. from Lab. Gen. Pathology, Univ. of Saratoff, 1925.

The work was done on the isolated hearts of dogs and cats. The heart was nourished in Ringer-Locke solution with the addition of 0.125% of sugar. Sugar determinations before and after experimentation were made by Bertrand's method. The data indicate that extirpation of the **pancreas** leads to diminution of absorption (almost 3 times less) of sugar by the isolated heart; the same is true after **parathyroid** extirpation (almost 2 times less). Extirpation of the **thyroid** gland, the **thymus**, and especially the **suprarenals**, is accompanied by increased glucose absorptive power of the heart. On examination of combined insufficiency, an outstanding antagonism was observed between the pancreas group on the one hand and the thyroid and suprarenal capsules on the other. There appeared to be no effect from extirpation of **testicles** on exterior parathyroid. Subcutaneous injection of adrenalin causes less absorption of sugar by the heart. If adrenalin is added to the nutritive fluid (heart normal), the absorption is doubled. When **insulin** is added to the nutritive fluid (heart in normal state), the absorption increases 3 times or more. The absorption increases also in the heart of an animal with adrenal **diabetes** if adrenalin is added to the nutritive fluid. The isolated heart of an animal depancreatized but treated with insulin absorbs the glucose more than in the normal state.—M. W. C.

Constitution and cardiac changes in inanition (Die Herzensänderungen beim Hungern im Zusammenhang mit seinem konditionellen Besonderheiten als eines Organs). Stefko (W. H.), Ztschr. f. Konstit. (Berl.), 1924, **9**, 501-516.

It is concluded from a study of human material that cardiac hypoplasia and atonia of the vascular and muscular systems are apparently related to certain changes in the **gonads** and **adrenals**.

—A. T. R.

A case of dwarfism (Ein Fall von Zwergwuchs). Wetzel (R.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 211-228.

Physical and röntgenographic findings in a female dwarf 60 cm. high at 6 years of age. With the possible exception of some

hypophyseal disturbance, the endocrine organs appeared to be normal, although they were not intensively studied. Literature is cited.—A. T. R.

Continuation of secretion of the ovarian follicular hormone by the human corpus luteum. Allen (E.) & Doisy (E. A.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 303-305.

Studies with human material obtained at operation and tested on ovariectomized rats show that the follicular hormone is secreted after the formation of the corpora lutea. In swine and cattle the hormone has not been found in corpora lutea. The authors emphasize the fact that the follicular hormone acts on the vagina and uterus in the absence of the ovary and, therefore, influences these parts directly and not by way of the ovary.—J. C. D.

Influence of castration on motor nerve energy (Influence de la castration sur l'energie nerveuse motrice). Athanasiu (I.) & Pézard (A.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 874-876.

The action current of the gastrocnemius during voluntary walking is in capons only 20% of that in normal cocks. The nervous system is more influenced by castration than is the muscular system.—A. T. C.

Significance of the right rudimentary genital gland in the hen (Sur la signification de la glande génitale rudimentaire droite chez la Poule). Benoit (J.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 341-344.

Since **ovariotomy** in hens leads to development of a testis with complete spermatogenesis at the expense of the right rudimentary sexual gland (called at present the right rudimentary ovary), this should be considered as a rudimentary **testis**.—A. T. C.

Endocrine activity of the young testis in fowls (Sur l'activité endocrine du testicule impubère chez les Gallinacés). Benoit (J.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 881-883.

Testes in even the 20-day chick condition the growth of the comb.—A. T. C.

A new case of experimental sexual inversion in the domestic fowl (Sur un nouveau cas d'inversion sexuelle expérimentale chez la poule domestique). Benoit (J.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 1640-1642.

Removal of **ovaries** caused development of sexual organs of male character, and of secondary sex characters.—A. T. C.

Stimulation of the surviving rabbit uterus by serum of pregnant and parturient women (Die Erregung des überlebenden Kaninchenuterus durch Schwangeren- und Kreisendenserum). Brdiczka (G.), Arch. f. exper. Path. u. Pharmakol. (Leipz.), 1924, **103**, 188-195.

The serum of parturient women, also juice expressed from the **placenta**, produce strong contractions and a very definite increase in the tone of the isolated rabbit's uterus. The same effect is produced by serum from the blood of women in the 9th and 10th months of pregnancy; serum taken during the 6th and 7th months is relatively ineffective. Reasons are given for assuming that the activating substance is not **adrenalin**, but an as yet unidentified body formed in the placenta.—Med. Sc., **11**, 259.

Lipoid metabolism in the ovary with regard to the menstrual cycle together with investigations on the adrenals and mammary gland (Der Lipoidstoffwechsel der Ovarien mit besonderer Berücksichtigung des Menstruationszyklus nebst Untersuchungen an Nebennieren und Mamma). Berberich (J.) & Jaffé (R.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 1-27.

A study based on material from women and cows. The largest amount of lipoid (cholesterinesters and cholesterin-fatty acid mixtures) in the **corpus luteum** of menstruation is reached when the granulsoa is at its highest, i. e., about 3-4 weeks after ovulation. Fatty acids and soaps are found only in atresia. Acute diseases have no influence. Amenorrhea due to chronic diseases may finally result in a total loss of ovarian lipoids. Cholesterin-fatty acid mixtures and cholesterinesters are regarded as merely storage products. The lipoid content of the adrenals is not related to the ovarian content. Literature is cited.—A. T. R.

Dental investigation in homosexual men (Gebissuntersuchungen an homosexuellen Männern). Dobkowsky (T.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 191-210.

The study is based on over one hundred cases, each of which is tabulated as to general sexual habitus and dental and gingival characteristics. The average size of the teeth of homosexual men lies between the normal male and female dimensions. There are more dental irregularities and decay in homosexual than in normal men. While the cause of these degenerative changes in the teeth and gingiva have frequently been attributed to dysfunction of the endocrine organs, Dobkowsky believes that the dental changes are due to the same factors that are responsible for the general homosexual constitution. Undoubtedly there is some relationship between these anomalies and the generative organs. Literature is cited.—A. T. R.

Etiology of hermaphroditism and other anomalies related to sex (Entstehung krankhafter Zwittrigkeit und anderer Störungen der geschlechtlichen Beziehungen. Kritik der Inkretionstheorie). Greil (A.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 121-190.

An extensive and critical examination of the subject shows that many etiological factors other than endocrine may be responsible for these anomalies. These include developmental irregularities, infections, intoxications, trauma during intrauterine life, severe nutritional disturbances in the mother, psychopathic conditions, etc. Literature is cited.—A. T. R.

Morphology and experimental investigation (gonad transplantation) in aged dogs (Morphologische und experimentelle Untersuchungen an alternden Hunden). Harms (W.), Ztschr. f. Anat. u. Entwcklngsgesch. (Berl.), 1924, **71**, 319-381.

The endocrine glands in general **(thyroid, hypophysis, adrenals)** showed evidences of hypofunction, and degeneration was usually present. The gonads showed the usual senile changes, the interstitial cells of the **testis** being well preserved. Transplantation of sex glands in several old animals was followed by evidences of rejuvenescence with evidences of regeneration in the gonads. Section of the vas deferens is not considered safe. Literature is cited.
—A. T. R.

A reaction of the testicular hormone (Sur une réaction de l'hormone testiculaire). Lagrange (E.), Compt. rend. Acad. d. sc. (Par.), 1924, **179**, 923-924.

Successive injections of 0.1 to 0.2 of fresh rabbit's testis into adult female rabbits produce after some days atrophy and discoloration of the **ovaries** (which vary between 37 to 130 mg., instead of 125 to 800 mg.). Sterility sets in between 15 to 20 days, and lasts 6.5 months. The **corpus luteum** atrophies. If the female is impregnated previously, these results do not follow. The effects are transitory. They are not produced by testes from other species injected into rabbits.—A. T. C.

Onychauxis in a eunuchoid. Remarkable improvement following implantations of testicular substance. Lisser (H.), Arch. Dermat. & Syph. (Chicago), 1924, **10**, 180-182.

This is the report of the case of a man of 31 whose testicles had atrophied as a result of an accident 11 years previously. When seen he had become eunuchoid, was mentally sluggish, and had physical inertia. The distribution of hair was feminine in type, and the nails showed onychauxis, that is, simple thickening. He

was still potent, and libido also was present to a fair degree. He had been treated with **thyroid**, anterior lobe of **pituitary**, and testicular extracts, singly and in combination, by mouth before being seen by Lisser. He had derived, according to his own statement, some slight and transient benefit from such treatment, but it had effected no improvement in the nails. A piece of fresh ram's testicle was implanted into the abdominal wall of the patient. This was followed by a gain of 5 lbs. in weight, marked increase in the size of the patient's testicular remains, and a subjective sense of well being and increased strength. He now was able to work fairly continuously for a year and a half, whereas previously he had been unable to hold a post for more than a week or two. The nails became somewhat smoother during this time. Twenty-one months later, after he had had a nervous breakdown, partly due to domestic troubles, a teaspoonful of semi-solid ram's testicular substance was forcibly injected subcutaneously into the abdominal wall. The patient gained 7 lbs. in the first week following this procedure. He gained strength and returned to work. Three more similar injections were given in the next 12 months. No unpleasant local or general reactions occurred, and the injected material was gradually absorbed between treatments. At the end of this time the finger nails had become entirely normal and the toe nails nearly so. No local treatment had been given to the nails. The article is illustrated with 3 photographs showing the nails before and after treatment. Two references to the literature are given.
—Med. Sc., **11**, 75.

Lipoids in the testes in general affections (Die Hoden bei Allgemeinerkrankungen). Lotz (A.) & Jaffé (R.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 99-110.

A histological study of 55 pairs of fully developed human testes with special reference to the lipoid content. In general the amount of phosphatides and cerebrosides in the intratubular tissue is greater than the amount of cholesterinester and cholesterin compounds. In the interstitial cells the relative proportion of these two classes of compounds is reversed. In the aged the intratubular phosphatides and cerebrosides may entirely disappear. In **diabetes mellitus** there is a decrease in all the intratubular lipoids and in the phosphatides and cerebrosides in the intertubular tissue. There is no correlation between the testes and the **adrenals** with reference to the weight or lipoid content.—A. T. R.

Survival of the mammalian testis in vitro. Lundy (C. J.), J. Am. M. Ass. (Chicago), 1925, **84**, 746-748.

Lundy has endeavored to determine the length of time that may be permitted between the removal of the testis from the donor and a successful graft made into the recipient. He transplanted slices of testis tissue as well as the whole testis of adult white rats immediately after, 24 hours after, 48 hours after, and 72 hours after removal from the donor. The site of transplantation was in the scrotal sac within the tunica vaginalis. Autoplastic and homoplastic transplantations were made into completely castrated male animals. Observations on the motility of the spermatozoa were made immediately, 24, 48 and 72 hours after removal of the testes from the donor, warmed to 37° C., and examined by the hanging drop method. Twenty-four hours after removal of the testes from the body a few of the spermatozoa were slightly motile. Instead of darting back and forth, they remained in the same relative position, and their tails moved sluggishly from side to side. Forty-eight hours after removal no motility was observed. As to the viability of the testis tissue of the rat, it was found that when preserved 24 hours or longer outside the body, it cannot be used for successful transplantation.—A. M. A.

Lipoids in testes of children (Lipoiduntersuchungen im kindlichen Hoden). Oppermann (E.) & Jaffé (R.), Ztschr f. Konstit. (Berl.), 1924, **10**, 111-120.

A study based on the testes of over 50 boys, from newborn babies to 16 years of age. Only small amounts of glycerinesters were found in the interstitial cells during the first two weeks of life. In children from 1 to 9 months of age that died of acute diseases the abundant interstitial cells contained also cholesterin and fatty acid compounds. In marasmus the authors found glycerinesters instead of cholesterinesters, while in accidental death (all over 2 years of age) no lipoid was found in the interstitial cells. However, when the germinal epithelium begins to mature in such cases, phosphatides and cerebrosides appear in these cells. In chronic diseases the abundant intertubular tissue is free from lipoid-containing interstitial cells. The authors do not believe in the trophic function of the interstitial cells.—A. T. R.

The production of certain distinct types of reactions by the use of ovarian extracts. Papanicolaou (G. N.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1924, **22**, 106-108.

Corpora lutea of pigs and cows were used and the extract tested on guinea pigs, particularly by watching the changes in the estrous cycle. Three effects were noted, produced presumably by three different hormones. (1) Extracts of corpus luteum of a lipoid nature

suppress the ovulation and otherwise simulate the effect of the developing corpora lutea in the animal's own ovary. (2) Ovarian and follicular fluids and ovarian residue extracts give the results described by Allen and Doisy. They produced typical estrous changes in the uterus, vagina, etc. (3) Water soluble fractions of alcoholic extracts of whole ovaries and corpora lutea have a stimulating effect on the ovary, regulating estrous, but not producing directly the estrous changes in the genital tract. All three types of extract are effective when injected. The last type of extract is the only one showing any activity when taken by mouth.—J. C. D.

Lipoid investigations on cattle testes (Lipoiduntersuchungen am Rinderhoden). Sorg (K.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 67-78.

A histological study of 25 pairs of testes from animals varying in age from 8 days to 5 years (extra uterine). Lipoid-containing interstitial cells are first regularly seen after the fourth week. From puberty on, similar lipoid (phosphatides and cerebrosides) accumulates in the germinal epithelium. Sorg concludes that the lipoid in the germinal epithelium constitutes an essential part of the cells, while in the interstitial cells it is merely a storage product and is evidence that the interstitial cells are related to other endocrine organs, e. g., **adrenal** cortex, in connection with lipoid metabolism. Literature is cited.—A. T. R.

Secondary ascent of the testis in starvation during childhood (Über das sekundäre Hinaufsteigen der Hoden beim Manne während der Kinderzeit). Stefko (W.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 289-306.

Stefko presents considerable evidence from a study of many hundred starved children that the excessive number of cases of cryptorchism in boys under these conditions is due to a secondary ascent of the testis caused by a reduction in the cremaster musculature, which accompanies the general underdevelopment of the abdominal musculature.—A. T. R.

Lipoid content in the follicular apparatus of human and cattle ovaries (Untersuchungen über den Follikelapparat der Ovarien bei Mensch und Rind, mit besonderer Berücksichtigung der in ihm auftretenden Lipoide). Yamauchi (M.), Ztchr. f. Konstit. (Berl.), 1924, **10**, 28-66.

The relative amount and character of the lipoid found in various tissues of a large number of human ovaries from newborn to adult subjects and of cattle ovaries from 2 weeks to 8 or 10 years

of age is tabulated. The results are much alike in the two species. —A. T. R.

A case of Fröhlich's syndrome. Abrahamson (L.), Irish J. M. Sc. (Dublin), 1925, 5s. No. 37, 58-62.

The case, that of a 17-year-old boy, appeared to be typical except that the sugar tolerance instead of being increased was distinctly diminished.—R. G. H.

The effect of pituitrin on blood and on lymph and urine production. Bayley (E. C.), Davis (J. C.), Whitman (W.) & Scott (F. H.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 312-314.

In 20 dogs tested with pituitrin injections, the blood concentration changed but slightly. The flow of lymph from the thoracic duct was very markedly decreased. The flow of urine was reduced and then markedly increased. These results indicate that the capillaries and kidney cells were rendered less permeable but that in the kidney the increased blood pressure eventually more than counterbalanced this.—J. C. D.

Purine metabolism in diabetes insipidus (Sur le métabolisme des purines dans le diabète insipide). Eliane Le Breton & Kayser (C.), Compt. rend. Acad. d. sc. (Par.), 1924, **179**, 1218-1219.

The excretion of purines other than uric acid parallels the degree of polyuria, and the ratio of uric acid to hypoxanthine is smaller, the more intense the polyuria.—A. T. C.

Juvenile adiposity. Engelbach (W.), Ann. Clin. Med. (Balt.), 1924, **3**, 198-208.

This paper describes a series of cases of juvenile adiposity shown before the American Congress of Internal Medicine. The condition, it is pointed out, is extremely common, but, as children do not tend to suffer from any other complaints at this age, except their physical abnormality, it is often left untreated. Good results can be obtained in pituitary cases by treatment with pituitary extract, and the author claims that the results obtained in one-third of his cases are as striking as those produced by **thyroid** administered in **myxedema.** They are not, however, so constant on the whole, for the late diagnosis and late institution of treatment, often many years after the gland has begun to function abnormally, preclude this. He suggests that 70-80% of cases of juvenile adiposity are of pituitary origin, and that the real importance of the adiposity at this age is not so much the cosmetic effects or inconvenience of overweight as the danger signal indicating insufficiency of the

anterior lobe, which controls to a large extent the osseous growth and the development and function of the genital system. Consequently such obesity should be regarded as a suspicious sign and treatment should be instituted. If this were done, the author suggests that the number of individuals who go through the adolescent period without proper development and function of the generative organs would be considerably diminished.—Med. Sc., **11**, 168.

Secondary female hirsuteness, a hypophyseal characteristic (Die sekundäre weibliche Behaarung, ein Hypophysenmerkmal). Olivet (Jeannet), Ztschr. f. Konstit. (Berl.), 1924, **10**, 268-280.

From clinical cases and experimental evidence, Olivet concludes that the "male" type of hair distribution over the face and body is a specific sex characteristic dependent upon the testes, while the "female" type (finer and less extensive) is really an asexual type, development of which is dependent upon the hypophysis and hence is modified in hypophyseal disorders. Literature is cited.—A. T. A.

A clinical study of deficient anterior pituitary functioning in women. Perkins (J.), Boston M. & S. J., 1924, **191**, 973-977.

Thirty-one cases are tabulated to show the occurrence in them of different symptoms. Anterior lobe substance apparently gave relief in some of these cases.—J. C. D.

Blood sugar studies in experimental pituitary and hypothalamic lesions. Sachs (E.) & MacDonald (M. E.), Arch. Neurol. & Psychiat. (Chicago), 1925, **13**, 335-368.

An experimental study of blood sugar values in the dog following removal of the hypophysis and lesions of the hypothalamic region was carried out. The lateral approach of Cushing and Paulesco was used. Protocols of 35 operated animals are reported, with blood sugar values, blood sugar tolerance curves, urinary findings, clinical symptoms and postmortem histologic findings. The experiments indicated that complete removal of the pituitary, if the hypothalamus is not injured, does not lead to the death of the animal. Deaths that occurred were always associated with hypothalamic injury. These experiments confirm the work of others that polyuria is apparently due to hypothalamic injury. The blood sugar average in fasting animals is slightly lower after pituitary or hypothalamic operation, but this may be within normal limits of variation. Transient glycosuria for from one to two days occurred after hypothalamic puncture in a few cases, and during this time the blood sugar was higher than normal. Because of the transience of this symptom, the investigators do not consider it of

great importance. The height of the blood sugar curve following operation, in all cases except those of anterior lobe removal, was reached at the end of one hour, in contrast to the curve in normal animals in which the height occurs at the end of one-half hour. The blood sugar curve in the cases of anterior lobe removal was of the normal type. The authors were unable to produce permanent glycosuria experimentally, although it has been observed in cases of pituitary disease. Some, but not all, of these were cases of hyperfunction of the anterior lobe, which, it is stated, can not be produced experimentally.—R. G. H.

Changes in the hypophysis in chronic inanition (Über die Änderungen in der Hypophyse bein chronischen Hungern). Sedlezky (S. K.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 356-366.

The developing human hypophysis in chronic inanition, which in general was an accompaniment of various serious diseases, shows loss in weight of the organ as a whole, hypoplasia of the glandular portion, reduction in eosinophilic cells and an increase in colloid. The necrosis in the pars anterior is characterized by basophilic granulation. The basophilic cells increase. Hyperemia is evident. Most of these changes also occur in the fully developed hypophysis in chronic inanition. However, only about 20 cases of all ages were observed. Post-mortem examination was made one and two days after death and the weights of other organs, including most of the ductless glands, are tabulated. Some literature is cited.

—A. T. R.

Further studies on the bio-assay of pituitary extracts.—The action of standard infundibular powder on the secretion of urine. Smith (M. I.) & McClosky (W. T.), J. Pharmacol. & Exper. Therap. (Balt.), 1924, **24**, 371-389.

A desiccated and defatted infundibular powder was found to have renal effects similar to the fresh gland extract. In anesthetized rabbits the augmentation lasted about one-half hour, often preceded by a short period of urinary suppression and sometimes followed by a more lasting diminution of flow. In non-anesthetized animals and in the human subject pituitary extract produced a more lasting diminished urinary output.—G. E. B.

On the dialysis of the physiologically active constituents of the infundibulum. Smith (M. I.) & McClosky (W. T.), J. Pharmacol. & Exper. Therap. (Balt.), 1924, **24**, 391-403.

The diffusion rates of the oxytocic, pressor and renal principles in infundibular extracts were found to be similar. This further indicates their chemical identity as held by Abel.—G. E. B.

Cessation of diabetes insipidus on roentgen-ray treatment of pituitary gland. Towne (E. B.), J. Am. M. Ass. (Chicago), 1924, **83**, 2085-2087.

The evidence presented suggests that a cure of diabetes insipidus was effected as a result of recession of a pituitary tumor under roentgen-ray treatment. It is said to be the first case of the kind on record. This patient suffered from diabetes insipidus, associated with one definite sign of a lesion in the vicinity of the optic chiasm—a defect in the upper temporal quadrant of the right visual field. A diagnosis of pituitary tumor was made, and the patient was treated by roentgen-ray crossfire to the pituitary region, in hope of causing recession of the tumor. Three months later the visual fields had returned to normal and have remained so. The urinary output dropped from about 8 liters to about 3.5 liters in the first three months; there was a recurrence at the fifth month which again appeared to respond to the roentgen ray; and there was another recurrence and similar, though slower, response beginning in the eighth month. Seventeen months after treatment was started, the output dropped to 2.5 liters, and it has remained at about that point until the present time, over three years after the patient came under observation. Very striking improvements and relapses in the physical and mental condition of the patient coincided with the drops and rises of the urinary output. The net result, clinically, is that a totally incapacitated man has become an efficient wage-earner.

—A. M. A.

Therapeutic uses of the parathyroid gland. Berkeley (W. N.), Boston. M. & S. J., 1925, **192**, 296-298.

From observations on several hundred cases made by different physicians and covering a period of 19 years, the author claims that parathyroid medication is distinctly helpful in paralysis agitans.

—J. C. D.

Disappearance of an old genital atrophy after ingestion of large quantities of fresh thymus (Disparition d'une atrophie génitale ancienne après ingestion de grandes quantités de thymus cru). Camus (J.) & Gournay (J. J.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 673-674.

A dog with experimental **diabetes insipidus** from a lesion at the base of the cerebrum showed after 4 years considerable obesity and complete genital atrophy. Feeding fresh thymus led to no change in weight or in the degree of polyuria, but the genital atrophy disappeared.—A. T. C.

A case of tetany treated with parathyrin. Collip (J. B.) & Leitch (D. B.), Canad. M. Ass. J. (Toronto), 1925, **15**, 59-60.

A female child, aged 22 months, with pronounced rickets, developed characteristic tetany during an attack of broncho-pneumonia. "Parathyrin," given daily subcutaneously and then by mouth, caused disappearance of all signs of tetany within 24 hours. There was no sign of recurrence during 14 days' treatment and 7 subsequent days without treatment.—A. T. C.

Perlingual administration of insulin (L'administration perlinguale de l'insuline). Blum (L.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 1225-1226.

Positive results (lowered hyperglycemia) are produced with extremely concentrated preparations, but are less constant than when insulin is injected.—A. T. C.

Generalized edema immediately following insulin control in diabetes mellitus. Gibson (R. B.) & Larimer (R. N.), J. Am. M. Ass. (Chicago), 1925, **84**, 491-492.

A pronounced generalized edema occurring in diabetic patients immediately following desugarization of the urine with insulin therapy was observed five times last year in the clinic with which Gibson and Larimer are connected. The edema promptly disappeared after treatment with potassium bicarbonate and potassium chlorid, 0.6 gm. each, three times a day, with meals. No recurrence of the edema had been reported by the patients when the potassium therapy was discontinued on discharge. None of the patients had significant renal or cardiac disturbances. The urines of all the patients were free from acetone and diacetic acid when the edema developed. That the edema may persist for thirty days if uncontrolled was shown in one case; potassium therapy was then instituted, and the edema almost completely subsided in thirty-six hours.—A. M. A.

Administration of insulin by mouth especially from the point of view of the age of the patients and the condition of the stomach (De quelques essais d'administration de l'insuline par voie buccale spécialement au point de vue de l'âge des patients et de l'état fonctionnel de l'estomac). Gjertz (E.), Acta med. Scand. (Stockholm), 1925, **61**, 295-300.

The experiences of 6 patients are reported, 3 diabetics ranging in age from 9 to 21 years, and 3 others, aged 41 to 47 years, having achylia gastrica or diminished HCl. Two of the latter were dia-

betics also. A marked difference was noted between the two groups. Three hours (in one case only 2 hours) after ingestion of insulin in oil or in water the blood sugar was lowered in those of the first group 0.040 to 0.058 per cent, while in the second it was lowered only 0.016 to 0.020 per cent. This cannot be explained merely by the different reaction of the two groups to fasting. It is shown that in young diabetics insulin causes diminution of sugar in the blood when a similar diminution is not manifested in older patients and those in whom the gastric secretion is altered. Larger doses of insulin were administered to one patient in each of the two groups to determine whether larger doses of insulin would cause greater diminution of the blood sugar. Uniform results were not obtained, however.—Author's summary.

Does insulin significantly affect the blood concentration? Hamilton (W. F.), Barbour (H. G.) & Warner (J. H.), J. Pharmacol. & Exper. Therap. (Balt.), 1924, **24**, 335-337.

Convulsive doses of insulin given to normal dogs and rabbits failed to alter materially the total solids or the specific gravity of the blood.—G. E. B.

Action of insulin on the basal metabolism of the totally depancreatized dog (Action de l'insuline sur le métabolisme basal du chien totalement dépancréaté). Hédon (E.) & Hédon (L.), Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 1633-1635.

A five months' experiment with a totally depancreatized dog showed that if insulin treatment with proper diet be sufficiently prolonged a normal condition of nutrition can be completely restored.

A. T. C.

The action of insulin in the frog and some vertebrates. Hemmingsen (A. M.), Skandin. Arch. f. Physiol. (Leipz.), 1924, **46**, 56-63.

The blood sugar of the frog is reduced after insulin injection. In butterfly larvae the total reducing power of the blood rises after giving insulin. In neither animal does it change the rate at which injected sugar disappears from the blood stream. No convulsions were observed. Two and one-half hours after injection of insulin into butterfly larvae the respiratory quotient rose, probably indicating an increase in carbohydrate metabolism.—G. E. B.

Some observations on insulin; its effect on the isolated heart and its therapeutic action (Einige Angaben über das Insulin: seine Wirkung auf das isolierte Herz und seine therapeutische Anwendung). Kogan (V. M.), Ztschr. f. d. ges. exper. Med. (Berl.), 1924, **42**, 25-40.

Many observers have studied the antagonism existing between **adrenalin** and insulin in their effect on the blood sugar. Experiments have also been carried out on the influence of insulin on the isolated heart, but though an increased removal of sugar from the circulating fluid has been shown, no effect on the heart's beat has been previously noted. The author has now studied the action of insulin on the heart, and finds that there is a marked influence on the beat, the systolic amplitude being increased and the pause lengthened. Adrenalin and insulin are not only antagonistic, therefore, in their effect on blood sugar, but also in their action on the beat of the heart.—Med. Sc., **11**, 97.

Theory of insulin action (Theorie der Insulinwirkung). Laufberger (V.), Klin. Wchnschr. (Berl.), 1925, **4**, 151-154.

Laufberger shortened the life of rabbits poisoned with insulin by forcing them to run. Frogs kept for 14 hours daily at a temperature of 24 C. died within 4 days when injected daily with one-tenth of the dose necessary for a rabbit. Frogs kept in a cool room showed no disturbance after 20 days, but died in about 3 hours when brought into a warm room. The increased amount of lactic acid in the blood depends on the exertion and not on the action of insulin. The phenomenon can be demonstrated also on isolated extremities of an animal. Insulin does not inhibit the formation of glycogen from glucose and dioxyacetone. It prevents the change of proteins and fats into glucose. The respiratory quotient after ingestion of a mixture of alcohol and glucose is not influenced by insulin. This indicates that it does not enhance the oxidation of sugar. The increased utilization of sugar by the surviving heart and the increased respiration of tissues after insulin are admitted. Yet the author points out that other substances—especially other hormones—produce the same effect in isolated tissues. The really specific action of insulin can be observed only on the whole organism. No proof of an increased cleavage of carbohydrates in the intact organism by insulin has been presented. Its inhibiting action on the new formation of carbohydrates from other substances is, in his opinion, the essence of its action.—J. Am. M. Ass., **84**, 861.

The effect of insulin on the morphological blood picture. Levine (V. E.) & Kolars (J. J.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 169-170.

In rabbits there is an increase in the number of red and white cells per cc. after insulin. The increase of the white cells is proportionately greater than that of the red. The change in count follows

the fall in blood sugar. Anhydremia with mild leucocytosis would account for these changes.—J. C. D.

Diabetic cataracts in an infant. Major (R. H.) & Curran (E. J.), J. Am. M. Ass. (Chicago), 1925, **84**, 674.

Major and Curran report the case of a boy, aged 11 months, who was admitted to the hospital because of the presence of sugar in the urine. Six months before admission, the mother noticed that the child became restless, and that his eyes began to get dark and were changed in appearance. The physical examination showed marked emaciation. The skin was somewhat yellowish. He was very fretful and cried constantly. Both eyes showed a marked lateral nystagmus, and the lenses of both were almost opaque and milky white in appearance throughout, excepting that there were two small areas in the left lens which were a little clearer than the rest of the lens. These ultimately became opaque. This patient was placed on a diet of whole cow's milk, 5% vegetable purèes and cod liver oil, and was given from 6 to 10 units of **insulin** a day A discission of each cataract was done, and the nucleus lifted into the anterior chamber to facilitate absorption. The cataracts had the appearance of those found in young diabetic patients and were certainly not congenital in origin, for as time went on they became denser. Six months later the patient was readmitted to the hospital, and at that time showed complete clearing up of one of the cataracts and almost complete disappearance of the other. The vision was apparently normal; the nystagmus had disappeared. Three blood sugar determinations showed 67, 127 and 80 mg. per hundred cubic centimeters. The boy at this time was taken off insulin. Recent letters from the patient's mother state that he is getting along very well with slight restrictions of diet and small doses of insulin, from 2 to 3 units a day. This is apparently the youngest diabetic patient on record suffering from cataracts. Other very striking features of his illness were the rapid increase and equally rapid lowering of tolerance from time to time.—A. M. A.

Insulin and galvanic excitability (Insulin und Galvanische Erregbarkeit). Waltner (K.), Klin. Wchnschr. (Berl.), 1925, **4**, 168.

Waltner tested the galvanic excitability of six children ranging in age from 11 months to 10 years. All had "cathode opening contraction" greater than 5 M. A. Under the influence of insulin along with decrease in blood sugar appeared an augmentation of the galvanic excitability. These in general ran parallel, though the effect

on excitability came on somewhat more slowly and lasted somewhat longer. The mechanical excitability was similarly affected.—R. G. H.

Some cases of diabetic coma complicated with uraemia, and some remarks on the previous history of the diabetic coma. Warburg (E.), Acta med. Scand. (Stockholm), 1925, **61**, 301-330.

The first case was described by v. Stosch in 1828. From a review of the literature and a metabolic study of 4 patients Warburg concludes that acute degeneration of the kidneys with great insufficiency occurs in some cases of diabetic coma. The albuminuria is often slight in these cases. The blood sugar is not infrequently extremely high, while the glycosuria is relatively low. Diacetic acid and acetone may be absent in these cases. In a number of cases the respiration is not of the "typical" hyperpnoeic form. The kidney degeneration is cured, at any rate partially, by insulin treatment. It is necessary to treat coma cases very early and very energetically in order to avoid cardiac and renal complications. Heart tonics and diuretics are of considerable value as adjuvants in conjunction with the pancreatic hormone. An excellent working bibliography is included.—R. G. H.

Hydremia of diabetes treated by insulin (L'hydrémie au cours du diabète traité par l'insuline.) Widal (F.), Abrami (P.), Weill (A.) & Laudat, Compt. rend. Acad. d. sc. (Par.), 1924, **178**, 2144-2145.

Insulin produces a definite upset of water equilibrium, with blood dilution, shown by fall of serum albumin. The effect sets in suddenly within 24 hours, and persists, although insulin treatment be stopped.—A. T. C.

Progressive and regressive forms of Hassall's corpuscles (Über progressive und regressive Formen von Hassallschen Körpern). Hammar (J. A.), Ztschr. f. Anat. u. Entwcklngsgesch. (Berl.), 1924, **70**, 466-488.

After giving a detailed description of the histological characteristics of both developing and degenerating forms of Hassall's corpuscles, Hammar lists Basedow's disease, various types of infection and snake bite (all characteristics of toxic factors) as conditions causing an increase in these corpuscles, probably from enlargement of reticular cells. Degenerated forms are noted especially in inanition and diseases caused by nutritional disturbances, as in cardiac failure, blood diseases, and perhaps also in epilepsy and eclampsia. Hammar stresses the significance of the regeneration of the corpuscles in connection with thymic function. Literature is cited.—A. T. R.

The presence and significance of lipoids in the thymus (Über das Vorkommen und die Bedeutung von Lipoiden im Thymus). Kyrilow (A.), Ztschr. f. Konstit. (Berl.), 1924, **10**, 460-481.

Kyrilow reports an investigation of the thymus from 34 cattle varying in age from 2 fetal months to 9 years, including 6 pregnant cows of the same age. In this species there are very few Hassall's corpuscles. Another unique feature is the presence of a special "infiltration cell." The author also examined 95 human thymus glands from premature and still-born subjects to persons past the climacteric stage, including 10 cases of pregnancy. Cholesterin mixtures in the intrathymic adipose tissue increases with age. Phosphatides are regularly present in Hassall's corpuscles. Fat is also found in certain reticular cells and eosinophilic leucocytes within the thymic parenchyma except during pregnancy. These fat-laden cells are also generally absent in climacteric women and those suffering from amenorrhea. There appeared to be no correlation between the lipoid content and the particular diseases, although in three cases of uremia unusually large fatty Hassall's corpuscles were present. Literature is cited.—A. T. R.

The treatment of the complications arising after operations on the thyroid gland. Clute (H. M.), Boston M. & S. J., 1924, **191**, 1147-1151.

The article is based on 1376 operations. The author concludes that although most patients have an uneventful recovery, those complications which may follow any surgical procedure occur at times in operations upon the thyroid gland. These complications are treated on the general surgical principles now well established. Complications arising from increased thyroid secretion should seldom arise if the proper operative procedure has been chosen. Mediastinitis is the most serious complication following thyroidectomy. Recurrent laryngeal nerve paralysis may rarely occur from injury to one nerve. A bilateral paralysis should never occur. Cases of hyperthyroidism should have repeated metabolism tests after operation in order to be certain that their metabolic rate is normal, as only in this way can we be certain that they are cured.—J. C. D.

Preparation of an antithyroid serum and its biological properties (Preparation d'un sérum antithyroïdien; ses propriétés biologiques). Coulaud (E.), Compt. rend. Soc. de biol. (Par.), 1925, **91**, 920-922.

Coulaud attempted to produce a cytolytic serum for the thyroid gland. Fresh sheep thyroid was ground finely in a mortar, using aseptic precautions, and physiological salt solution added. After

allowing the suspension to settle the supernatant fluid was injected intravenously into sheep 4 to 6 times at 2 day intervals. Serum obtained 45 days later had a marked effect on the thyroids of rabbits into which it was injected. It caused a disappearance of colloid and a reversion to the fetal condition. By the complement deviation method no antibody could be detected.—R. G. H.

The effect of iodine on hyperthyroidism in man. Cowell (S. J.) & Mellanby (E.), Quart. J. Med. (Oxford), 1924, **18**, 69.

The relationship between the iodine content of the thyroid gland and the occurrence of the symptoms of hyperthyroidism in man is discussed. Reports are given of a series of cases of hyperthyroidism treated with small doses of iodides. In every case clinical improvement was observed, accompanied by a fall in the basal metabolic rate and pulse rate. This improvement reached a maximum in from 10 to 20 days, and was then frequently followed by a gradual return of symptoms, which did not, as a rule, attain their former severity. The withdrawal of iodides from these patients, even when they had been receiving it continuously for several months, was followed by an exacerbation of symptoms which could be relieved by once more giving iodide. The authors conclude that in cases of hyperthyroidism the action of iodine is not merely concerned with the elaboration of thyroxin and the conversion of hyperplastic thyroids into colloid-containing ones, but that it influences metabolic processes in ways not at present understood.

—Physiol. Abst., **9**, 540.

Myxedema heart. Fahr (G.), J. Am. M. Ass. (Chicago), 1925, **84**, 345-349.

Fahr states that in myxedema there are definite objective signs as well as subjective symptoms of heart failure which may be present for many years, and which do not respond completely to the therapy of rest and digitalis but which are cured by thyroid medication. Characteristic of "myxedema heart" are an enormous dilatation of all chambers of the heart and absence of negativity of the T wave of the electrocardiogram in Lead I. The dilatation of the heart disappears rapidly, and the T wave becomes positive under thyroid medication. During the transition from a negative to positive T wave, we may get a stage in which the T wave is diphasic. A few cases show the split and prolonged Q-R-S group of delayed intraventricular conduction. This abnormality also disappears under thyroid medication. All of our patients showed a negative Q-R-S group in Lead III during the stage of marked cardiac dilatation. The negative Q-R-S group in Lead III, thought by many to be char-

acteristic of left ventricular hypertrophy, becomes positive in these cases after thyroid medication, thus proving for these hearts that a negative Q-R-S group in Lead III is not due to a preponderance of musculature of the left ventricle.—A. M. A.

Thyroid and nitrile poisoning (Schilddrüse und Nitrilvergiftung). Gellhorn (E.), Arch. f. d. ges. Physiol. (Berl.), 1923, **200**, 571-582.

Experiments with KCN, acetonitrile and propionitrile resulted in no support for a detoxication theory of thyroid function, since thyroidectomized mice showed greater resistance to KCN and propionitrile than normal controls. Acetonitrile is not a specific reagent for thyroid activity, since feeding thyroid, pituitary or testicular hormones also increases resistance to this poison.—A. T. C.

The influence of intestinal bacteria upon the thyroid gland. Harries (D. J.), Brit. M. J. (Lond.), 1923, **i**, 553-555.

The flora of the intestine can be subdivided into two groups, acid producers and indole producers. The indole producers are absent in exophthalmic and present in parenchymatous goiter, but in the latter the effects appear to be the result of the inability of the thyroid to use the material at its disposal rather than an undue destruction of tryptophane.—Physiol. Abst., **9**, 540.

The inverse relation of iodin and goiter in Utah. Hathaway (J. C.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 183.

Utah is on the edge of the goiter belt. It is found that the incidence of goiter in school children bears an inverse relation to the amount of iodin in the drinking water.—J. C. D.

A case of hypernephroma associated with thyroid hyperactivity. Kaufmann (J.) & Cashin (M. F.), Canad. M. Ass. J. (Toronto), 1925, **15**, 37-40.

As the hypernephroma extended the thyroid, already unbalanced by an adenoma, became suddenly toxic. Death occurred from thyroid hyperactivity and hypernephroma, toxicity of the one progressing proportionally to the destruction of the other.—A. T. C.

A quantitative study of the physiologic action of thyroxin. Kendall (E. C.), Proc. Soc. Exper. Biol. & Med. (N. Y.), 1925, **22**, 307-308.

An analysis of the structural formula of thyroxin as related to its oxidizing action. The function of thyroxin is to furnish a compound that can be acted on by mild oxidizing agents, among which is molecular oxygen, and which can then by an intramolecular rearrangement produce an intensely oxidizing substance.—J. C. D.

Studies on compensatory hypertrophy of the thyroid gland. Loeb (L.) & Kaplan (E. E.), J. Med. Research (Bost.), 1924, **44**, 557-578.

This paper describes a series of experiments which were carried out to throw further light on the relationship between the thyroid gland and the anterior lobe of the pituitary. Evidence that such a relationship does exist rests on two sets of observations and experiments: (1) those concerning the effect of the extirpation of one gland upon the other; (2) those concerning the effect of the administration of these glands on metamorphosis in amphibia. These experiments have shown that in amphibia the anterior lobe of the pituitary increases growth, and that even oral administration of this substance is effective; also that the anterior lobe of the pituitary contains a substance which hastens metamorphosis in amphibian larvae. After studying this evidence, the possibility was suggested to the authors that the administration of anterior lobe of the pituitary might exert some influence on the hypertrophy of the thyroid gland which develops in the guinea pig after extirpation of the greater part of this organ. It was also thought that the effect of administration of anterior lobe of pituitary on compensatory hypertrophy of the thyroid might constitute a valuable indication of the relationship of these two glands. Consequently, the series of experiments described in this paper were undertaken. A comparison was made between the compensatory hypertrophy following extirpation of the greater part of the thyroid gland in control guinea pigs kept on ordinary food, and the hypertrophy in guinea pigs which, after extirpation of the greater part of the thyroid gland, were fed, in addition, daily with one 5 gr. tablet of anterior pituitary (Armour & Co.). The results of a large number of experiments are given in detail, and show that in the guinea pig the administration of anterior lobe extracts by mouth prevents entirely, or almost entirely, the compensatory hypertrophy of the thyroid gland, which in a considerable number of cases does follow the extirpation of the greater part of this organ. The authors suggest that this effect is not caused by the admixture of inorganic salts of iodine with the preparation, because, as they are proposing to show conclusively in a subsequent communication, iodine in inorganic form is unable to prevent compensatory hypertrophy in the guinea pig.

—Med. Sc., **11**, 257.

Iodin and goiter. McGuire (S.), South. M. J. (Birmingham), 1925, **18**, 87-91.

Following the use of Lugol's solution by mouth in 50 cases of exophthalmic goiter McGuire concludes that pre-operative mortality can be reduced and desperate cases can be converted into good

surgical risks. Preliminary ligation can be practically abandoned if iodin is administered. Post-operative hyperthyroidism can be controlled. The present low mortality of thyroidectomy can be reduced despite the acceptance of risks previously declined. Mild cases can be relieved of symptoms and possibly tided along until there is spontaneous cure without operation. Patients that have had relapse after operation can be benefited and perhaps cured.
—R. G. H.

The oculo-cardiac reflex and endocrinology. Oliver (J.), & Oliver (G. Y.), Edin. M. J., 1925, **N. S. 32**, 69-71.

Pressure on the eyeball changes the pulse rate, slowing it in vagotonic and increasing it in sympathotonic individuals. This is, in the authors' opinion, helpful in diagnosing hyperthyroidism and hypothyroidism.—J. C. D.

Roentgen ray therapy in thyroid disturbances (Indicaciones y contraindicaciones de la Roentgenterapia en los transtornos anatomofunctionales del tiroides). Piga (F.) & Larrú, Siglo méd. (Madrid), 1923, **71**, 837-840.

A bibliographic resumé of this subject is given, from which the deduction is made that roentgen ray therapy may be indicated in a great number of cases of hyperthyroidism. A careful study of the symptoms in many such cases, however, shows that this treatment is directed solely to hyperthyroidism and not to other accompanying symptoms which merit attention. In all such cases a study should be made of the basal metabolism, thus proving the efficacy of roentgen therapy. In cases of goiter with compressional disturbances, radiotherapy is of no avail. Surgical measures ought to be carried out without delay. When goiter is associated with hypertrophy of the **thymus** there is little hope in radiotherapy; treatment of the thymus is required.—E. B.

Pulmonary tuberculosis and exophthalmic goiter (Tuberculosis pulmonar y bocio esóftalmico). Piasco (N.), Rev. de hig. y de tuberc. (Valencia), 1923, 182, 189, 194.

The coexistence of pulmonary tuberculosis and exophthalmic goiter is seldom observed. On the other hand, pulmonary tuberculosis is often wrongly diagnosed as Graves' disease, due to symptoms of thyroid origin, such as tachycardia, palpitations, irritability, trembling, slight thyroid hypertrophy, etc. The author describes 6 cases of pulmonary tuberculosis and hyperthyroidism. In all of these cases it was noticed that the tubercular lesions became more pronounced with the appearance of thyroid hyperfunction.—E. B.

The effect of thyroidectomy on the calcium content of the blood serum. Rabinowitch (I. M.), J. Lab. & Clin. M. (St. Louis), 1924, **9**, 543-546.

A decrease in calcium content of the blood serum following thyroidectomy was noted in 26 cases. The decrease was not of sufficient degree to produce tetany. As no **parathyroid** tissue was found in the portions of the thyroid removed, the author concludes that the phenomena is due to trauma during manipulation in the parathyroid regions.—I. B.

The effect of iodin in exophthalmic goiter. Starr (P.), Walcott (H. P.), Segall (H. N.) & Means (J. H.), Arch. Int. Med. (Chicago), 1924, **34**, 355.

These authors studied the effect of Lugol's solution in exophthalmic goiter, administering 15 minims daily. Twenty-five patients were treated identically, and pathological reports of the thyroid gland were obtained from all but two. Hyperplasia without adenomata was observed. This proves that proper subjects were selected in order to test Plummer's views on the rôle of iodin in exophthalmic goiter as opposed to adenomatous goiter with hyperthyroidism. Eighty per cent of these subjects responded to iodin by a more or less extensive remission of the disease, as indicated by drop in basal metabolism and pulse rate and gain in weight. The remission was found to be often as rapid and as extensive as that following subtotal thyroidectomy. The authors believe that the iodin administered was the cause of the remissions. But iodin alone (as Lugol's solution) was not found to cure or suppress the disease permanently. After a patient has been taking iodin, a rapid rise of metabolic rate and increase of toxic symptoms will occur within one or two weeks if the iodin is stopped. Therefore if iodin is used as a pre-operative preparation, no gap between medication and operation should be allowed to occur. Several excellent charts are included, illustrating iodin remissions and post-iodin reactions on basal metabolic rate, pulse rate and weight.—H. L.

Chemical and histological studies of goiter with special reference to cases of Graves' disease following iodine treatment (Chemische und histologische Untersuchungen an Strumen, mit besonderer Berücksichtigung von Jodbasedowfällen). Tobler (T.), Mitt a. d. Grenzgeb. d. Med. u. Chir. (Jena), 1924, **37**, 622-640.

The intensive campaign waged in recent years against endemic goiter in Switzerland, though on the whole strikingly successful, has had certain ill effects, especially in adults. The excessive use of iodine by the general population, without medical control, has resulted in a considerable increase in the prevalence of Graves' disease. In the author's clinic the yearly admissions for this condition have risen from 6 to 40, and he is of the opinion that the

preparations at present employed for the prophylaxis of endemic goiter contain too large an amount of iodine. An analysis of the iodine content of 39 goiters removed at operation shows that the percentage of iodine was lowest in patients with true Graves' disease who had received no iodine medication, while it was very greatly increased in goiters removed from patients who had developed symptoms of hyperthyroidism as the result of intensive iodine treatment. In the latter group 10 gm. of the fresh gland showed on the average no less than 8.9 mg. of iodine, as compared with 0.09 mg. in goiters removed from patients who had developed Graves' disease spontaneously. Goiters from patients in whom symptoms of hyperthyroidism had resulted from iodine treatment present a variable histological picture. In the majority the characteristic features of Graves' disease are present, but others are absolutely indistinguishable from colloid goiters.—Med. Sc., **11**, 257.